Clinical commentary

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Electroconvulsive therapy for psychosis in a patient with epilepsy related to hypothalamic hamartoma

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ABSTRACT – Psychosis is more common in people with temporal lobe epilepsy than it is in the general population. Treatment can be difficult in these patients because of the complex interactions between antipsychotic and antiepileptic drugs. Some antipsychotic drugs also decrease the seizure threshold. We report the case of a 49-year-old man with a hypothalamic hamartoma, with a history of both gelastic and temporal lobe seizures. The patient was rendered seizure-free after three neurosurgical procedures but developed a drug-resistant paranoid psychosis. He was treated with electroconvulsive therapy (ECT). After two weeks with six stimulations that resulted in seizures, the psychiatric phenomena disappeared completely. There was no relapse of either the psychiatric symptoms or the seizures during the 42 months of follow-up. This case report suggests that ECT might be safe for psychosis in patients with a history of seizures that have previously been successfully treated with neurosurgery, although caution should be exercised in drawing general conclusions from a single case report.

Key words: psychosis, epilepsy, electroconvulsive therapy, hypothalamic hamartoma, temporal lobe epilepsy, temporal lobectomy

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Psychosis is relatively common in people with temporal lobe epilepsy (TLE) (Jensen and Larsen, 1979). According to the temporal relationship with seizures, psychoses of epilepsy may be classified as: *postictal* psychosis, which occurs within seven days of the last seizure of a cluster; *alternative* psychosis, in which the patient alternates between periods with seizure but without psychosis and seizure-free periods with psychosis; or *interictal* psychosis, which has no clear

relationship with seizures (Commission on Classification and Terminology of the International League Against Epilepsy, 1989; Sachdev, 1998). Interictal psychosis is difficult to differentiate from primary schizophrenia. However, Crowe and Kuttner reported that TLE patients with psychosis experience a higher frequency of positive symptoms than patients with chronic schizophrenia (Crowe and Kuttner, 1991). Patients with TLE are generally recognised as good candidates for epilepsy surgery (Jutila *et al*., 2002), but psychiatric disturbance may complicate the postsurgical outcome (Foong and Flugel, 2007).

In such patients who present with drug-resistant psychosis, there may be reluctance to treat with electroconvulsive therapy (ECT) because of the history of epilepsy.

Case study

In 2008, a 46-year-old man was admitted due to a subacute delusional state. He had a medical history of epilepsy but had been seizure-free for 16 months following three neurosurgical procedures. Furthermore, besides the recurrent delusional states, he had no prior psychiatric history and specifically denied having had features of depression, mania, obsessive-compulsive, phobic, or panic disorders. His parents reported that, during childhood, he had hyperkinesis, irritability, and difficulty in adapting at school. There was no family history of neurological or psychiatric disorder. At 10 years of age, he had a first convulsive seizure and two years later had episodes with altered consciousness, oral automatisms, and right hemifacial clonic movements, also of the upper limb. Later on, the patient described feelings of *déjà vu*, *déjà vécu*, pleasant feelings, and "pressure to laugh". The electroencephalogram (EEG) showed changes consistent with left-sided TLE. The MRI revealed a hypothalamic hamartoma, without any visible changes in the neighbouring structures. It was concluded that the patient had gelastic epilepsy due to the hypothalamic hamartoma, and that the seizures had spread to the left temporal lobe. At 27 years of age, he was treated with haloperidol, 15 mg daily, for hallucinations without delusional or suicidal thoughts and was not psychiatrically admitted.

The epilepsy was refractory to numerous antiepileptic drugs (AEDs) given individually, at various times and in various combinations (lamotrigine at 400 mg daily, carbamazepine at 800 mg daily, phenobarbital at 100 mg daily, vigabatrin at 1500 mg daily, clobazam at 30 mg daily, and zonisamide at 300 mg daily) (*table 1*). A preoperative assessment was carried out at 33 years of age with a psychiatric assessment revealing an independent anxiety disorder. Neuropsychological testing showed no attentional deficits and memory functions were within the normal range, except for a lower verbal memory score, relative to visual memory, due to left-sided TLE. Ten months later, a first acute delusional episode occurred, concurrent with a change in AED treatment, as well as a slight increase in the frequency of both gelastic and temporal seizures. The patient had auditory and visual hallucinations associated with persecutory, megalomaniac, mystical, and sexual ideation, as well as elated mood. Following this, AEDs were increased to carbamazepine at 800 mg daily and phenobarbital at 100 mg daily, and antipsychotic medication was introduced, namely clozapine at 450 mg daily, haloperidol up to 60 mg daily, and chlorpromazine at 200 mg daily. Haloperidol was progressively decreased to 15 mg daily and chlorpromazine maintained at 200 mg daily (*table 1*). Because the psychotic symptoms persisted, the preoperative assessment was aborted and the surgery was postponed.

In 2001, at the age of 39, the psychotic symptoms that had been evident in 1995 had completely regressed, but some symptoms of anxiety persisted. In the same year, unsuccessful gamma knife surgery was performed on the hypothalamic hamartoma. The seizures relapsed six months later with up to 150 gelastic seizures daily associated with major anxiety and inappropriate aggressive behaviour. AEDs and antipsychotic medication was adapted and two years later, an endoscopic lesionectomy was performed to complete treatment of the hypothalamic hamartoma. The psychiatric symptoms then disappeared and the patient resumed his work as a stationer. Treatment with clozapine was decreased after the acute episode and continued at the dosage of 50 mg daily. Because the dyscognitive temporal lobe seizures persisted, a third neurosurgical procedure was performed, namely temporal lobectomy at 45 years of age. This proved to be an effective treatment for the refractory temporal lobe seizures. The patient's maintenance treatment with low doses of clozapine and clobazam controlled his anxiety (Judd *et al*., 1989), psychosis, and mixed mood features.

In 2008, 16 months after the temporal lobectomy, antiepileptic treatment was slowly tapered to lamotrigine at 300 mg daily and clobazam at 15 mg daily. The patient was seizure-free and EEGs were unremarkable. However, one month prior to his admission to the psychiatric unit, he spontaneously stopped the antipsychotic treatment of clozapine at 50 mg daily.

The psychiatric symptoms on admission were as follows: he compared himself to a scud (a type of tactical ballistic missile) and presented again with megalomaniac, sexual, persecutory, and fantastical ideas; he claimed to be close friends with famous political personalities. These symptoms were associated with

Table 1. Summary of all antiepileptic drugs (AEDs) and antipsychotic treatments (ATPs) used.

AEDs	Dosage of AEDs	Antipsychotics	Dosage of ATP	Introduction	Stop
Clonazepam	10 mg per day			1982	1988
Carbamazepine	800 mg per day 800 mg per day			1988 1994	1993 1998
Valproic acid	2500 mg per day			April 1988	July 1988
Phénobarbital (Ortenal©)	100 mg per day 50 mg per day			April 1988 July 1988	July 1988 1994
Clobazam	20 mg per day 30 mg per day **15 mg per day**			1988 1994 2008 1994 2008	1994 2008 2008 **Current treatment**
Phénobarbital (Gardenal©)	50 mg per day 100 mg per day			1993 Sept 1994	Sept 1994 2008
Carbamazepine LP	800 mg per day			1993 Sept 1994	Sept 1994 Progressively decreased to december
Lamotrigine	400 mg per day **300 mg per day**			2001 2008	2008 **Current treatment**
Vigabatrin	1500 mg per day			1998	2001
Zonisamide	300 mg per day			2004	2007
		Haloperidol	15 mg per day 25 mg per day 60 mg per day decreased in 3 months to 15 mg 10 mg per day	Aug 1989 1990 1995 **2008**	1990 1995 1997 **Current treatment**
		Chlorpromazine	200 mg per day	1995	2001
		Clozapine	450 mgper day 50 mg per day 500 mgper day	1995 1995 2008	Acute episode 2008 2008

The current treatments are in bold type.

racing thoughts and a looseness of associations. He presented with a lack of inhibition and appeared anxious during the psychiatric interview. In summary, he presented with a manic episode with mood-incongruent psychotic features, which could be related either to a Mood Disorder Due to Medical Condition (according to DSMIV TR: 293.83) or to a psychiatric disorder such as schizoaffective disorder (295.70).

Treatment with intramuscular loxapine (100 mg) was immediately administered. After the injection, the patient presented with malaise and non-sustained myoclonic-like movements, but EEG recordings and MRI remained unchanged. As the patient remained free of any additional seizures, he was not considered to have had a relapse of epilepsy. The psychosis did not improve and psychotropic treatment was increased to clozapine at 500 mg daily for more than three months

without efficacy and with a therapeutic plasma level of clozapine at 352 ng/mL. A trial of haloperidol at 10 mg daily resulted in no improvement and both clozapine and haloperidol were discontinued.

Because of the paranoid delusions and the manic symptoms, we proposed ECT treatment and reduced clobazam to 6 mg daily. In agreement with the patient's neurologist, bilateral ECT treatment (380 millicoumbs, three times per week) was started. After two weeks with six stimulations, each followed by a seizure, the psychiatric symptoms resolved completely. Haloperidol at 10 mg daily was reintroduced and clobazam increased to 15 mg daily. No further ECT was given. The current treatment consists of lamotrigine at 300 mg daily, clobazam at 15 mg daily, and haloperidol at 10 mg daily.

The patient had no psychiatric relapse or epileptic seizures during 42 months of follow-up, but did not resume his occupation.

Discussion

Electroconvulsive therapy has become well-established as a treatment for severe depressive disorders, manic states and, in some patients, refractory schizophrenia, essentially of paranoid type (Fink, 2004). In this patient, ECT might have been considered to be an inappropriate treatment because of the possibility of recurrence of the epilepsy. On the one hand, ECT-induced seizures may cause a relapse of the epilepsy; however, on the other hand, ECT appears to have an anti-seizure effect and may significantly increase the seizure threshold (Coffey *et al*., 1995). Some authors even suggested ECT as a treatment for status epilepticus (Lisanby *et al*., 2001; Cline and Roos, 2007). ECT was reported to be an efficient treatment of psychosis in patients with comorbid epilepsy (Micallef-Trigona and Spiteri, 2012; Anderson and Gadit, 2012). Furthermore, ECT appears to be effective in treating both the psychiatric symptoms and the epileptic seizures in some patients (Regenold *et al*., 1998; Kucia *et al*., 2007), as well as depression or catatonia in patients post-epilepsy neurosurgery (Kaufman *et al*., 1996; Maixner *et al*., 2010).

In the 1930s, Meduna developed the concept of antagonism between seizures and psychotic symptoms while using convulsive therapy to treat patients with schizophrenia, with some positive results (Fink, 2004). This phenomenon was subsequently termed "*alternative psychosis*"; when seizures are worse the psychosis improves and when seizures are controlled symptoms of psychosis worsen (Wolf and Trimble, 1985). The phenomenon of "*forced normalisation*" refers to the observation that the psychosis may be less apparent when the EEG is abnormal and worse when the EEG improves (Landolt, 1958). In this patient, the duration of the episode of psychosis implied a diagnosis of chronic *interictal* psychosis because the delay between the temporal lobectomy and the relevant psychotic episode was more than two years. The history of psychotic episodes before the surgery might suggest a diagnosis of schizoaffective disorder (295.70), but psychotic symptoms are also frequently associated with hypothalamic hamartomas (Veendrick-Meekes *et al*., 2007). The most appropriate psychiatric diagnosis in this patient appears to be Mood Disorder Due to Medical Condition (according to DSMIV TR: 293.83).

The neurophysiological mechanisms involved in the therapeutic effect of ECT are still unclear. Some hypotheses include a reduced neuronal excitability through the ECT-induced cortical concentration of GABA (Sanacora *et al*., 2003) or a modification of synaptic plasticity secondary to a form of long-term depression triggered by ECT (Kato, 2009). The psychopathogenesis of this particular psychosis associated with epilepsy remains unclear. Treatment can be difficult in these patients because of the complex interactions between antipsychotic and AEDs (Besag and Berry, 2006). Some antipsychotic drugs also decrease the seizure threshold (Alper *et al*., 2007).

This patient was successfully treated using ECT for a drug-resistant, sub-acute, psychotic episode. The use of ECT did not trigger a recurrence of the epilepsy. This case report suggests that ECT might be safe for the treatment of psychosis in patients with a history of complex partial seizures, successfully controlled with epilepsy surgery, although caution should be exercised in drawing general conclusions from a single case report.

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