Antiepileptic-induced Psychosis as a Possible Predictor of Post-temporal Lobectomy Alternative Psychosis

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Abstract

We present a patient with topiramate-induced psychosis who developed alternative psychosis following temporal lobectomy. The number of surgical candidates for temporal lobectomy is increasing as is the frequency of psychiatric co-morbidities. Preoperative planning should take account of these psychiatric co-morbidities. In particular, precautions should be taken when antiepileptic drug–induced psychosis occurs, as this could predict the occurrence of alternative psychosis following lobectomy.

Key words: Anticonvulsants; Electroencephalography; Epilepsy; Fructose; Seizures

Introduction

Epilepsy is a chronic and debilitating disease. Surgery in the form of lobectomy is often sought for patients in whom conventional antiepileptic treatment fails. Indeed, temporal lobectomy has become a recognised treatment for resistant epilepsies with remission rates post-lobectomy reported to be as high as 60 to 70%. Nonetheless, lobectomies are not without consequences. With the reduction in or complete disappearance of seizures, other complications arise, particularly major neuropsychiatric complications such as psychosis, depression, and anxiety. A large prospective study reported that patients who underwent temporal lobectomy for refractory epilepsy developed depression (22.1%) or anxiety (24.7%) postoperatively and could even develop schizophrenia-like psychosis. The mechanism of post-lobectomy psychosis has been postulated to be through alternative psychosis, whereby psychosis emerges after the seizures have been well controlled. Alternative psychosis, first described by Tellenbach, describes the clinical phenomenon of a reciprocal relationship between seizures and psychosis, without relying on electroencephalogram (EEG) findings. A similar concept, proposed by Landolt, is known as forced normalisation whereby the remission of seizures and absence of epileptiform activity on the EEG leads to psychotic episodes. Clearly, consideration of predictors of postoperative psychiatric morbidity is vital as such neuropsychiatric complications, particularly psychosis, can be debilitating. Among the predictors that have been reported are preoperative psychiatric disease, laterality of seizure focus, and age at the time of surgery. It is hypothesised that preoperative psychiatric disease, particularly depression, is indicative of more diffuse cerebral disease and worse seizure control. Nonetheless, little is known of antiepileptic-induced psychosis as a predictor of post-lobectomy psychosis.

To the best of our knowledge, this is the first case report to detail a patient who suffered from antiepileptic drug (AED)–induced psychosis pre-morbidly, and later developed post-lobectomy psychosis, with alternative psychosis as the likely underpinning mechanism.

Case Presentation

A 36-year-old female had suffered from epilepsy since 6 years of age. She had 2 to 3 seizures per day. Seizures started with blank staring and oral automatisms, with left upper limb dystonia and right head deviation. This was accompanied by drooling, up-rolling of the eyeballs, and postictal drowsiness for approximately 30 minutes. She had been suffering from epilepsy since childhood, but was only formally diagnosed in 2002 at the age of 23 years. Surgery to reduce the occurrence of seizures was suggested but she declined. With time, the frequency of seizures decreased to 2 to 3 times a week. She was initially prescribed carbamazepine and phenytoin, but later changed to levetiracetam as her seizures were not abating.
Levetiracetam was stopped and she was then switched to topiramate. Two weeks after commencement of topiramate, the patient started to experience auditory and visual hallucinations. She also had persecutory delusions whereby she believed her sister was trying to harm her and delusions of jealousy whereby she believed her husband was having an affair. While on topiramate, her seizures continued. The medication was subsequently stopped and her psychosis resolved a week later. A trial of antipsychotics was never tried at this point as her psychosis resolved with the removal of topiramate from her drug regimen.

Magnetic resonance imaging of the brain in 2002 showed right mesial temporal sclerosis. Video-EEG telemetry showed right anterior temporal interictal discharges and 9 focal seizures with right temporal ictal onset in 7 seizures. A positron emission tomographic scan of her brain showed right temporal hypometabolism. In view of her persistent and intractable seizures, a right temporal lobectomy was planned. She became seizure-free postoperatively. Two weeks later, a rechallenge was done with topiramate and she had no psychosis thereafter. Nonetheless, 1 month later she developed a psychotic episode. She became upset with her husband and believed that he was having an affair. Two days later she started experiencing auditory hallucinations, hearing a voice asking her to die and commenting that she was useless. Her voices were numerous, second person in nature and sometimes heard from afar. She also believed that others could read her mind. These psychotic symptoms only came to the attention of her treating doctor 8 months later, when her psychosis worsened. Olanzapine was commenced and within a week her psychosis improved. She was commenced on 15 mg once nightly olanzapine, and after 1 month her psychosis resolved completely. She remained seizure-free with medication and is currently in remission of her psychosis with olanzapine 5 mg once nightly.

Discussion

Epilepsy and psychosis have an interesting association that many authors have sought to understand. Understandably, psychosis associated with epilepsy is a major concern for neurologists and psychiatrists. Many patients with epilepsy develop psychiatric disorders, with some authors suggesting that psychosis in epilepsy is preferentially linked to temporal lobe epilepsy and that patients who have temporal lobe epilepsy are more apt to be psychotic.10,11

Although psychosis has been well described post-ictally, ictally, and interictally, there are now increasing reports of forced normalisation, particularly post-temporal lobectomy. Psychosis in epilepsy is attributed to a phenomenon known as kindling whereby repeated epileptiform discharges in the amygdala and ventral tegmental areas of the brain lead to plastic regenerative changes in the medial temporal lobes. Anomalous axonal sprouting from dentate granule cells has also been attributed in causing psychosis in epileptic patients.12 In alternative psychosis, amygdaloid and limbic kindling has been proposed as the mechanism that causes psychosis once seizures are well controlled.13 It is this antagonism that has piqued the interest of epileptologists and psychiatrists alike.

Temporal lobectomy has become a choice surgical procedure for intractable seizures, particularly those of the mesial temporal subtype.14 There have been positive reports of the procedure,15 but also of postoperative psychiatric adverse effects such as psychosis.11,16 The rate of psychosis after temporal lobectomy ranges from 3% to 28%, with the definitive underlying mechanism still elusive. One possible explanation is that the temporal lobe discharges could have an inhibitory effect on the limbic system and thus limbic dysfunction secondary to abatement of the temporal seizures could be responsible for the psychosis.17 It is thus interesting to study the notion that AED-induced psychosis could be a predictor of post-lobectomy alternative psychosis or forced normalisation.

Topiramate is a frequently prescribed AED in patients with refractory epilepsy.18 Unfortunately a number of published reports have cited adverse psychiatric effects of topiramate, particularly in patients with epilepsy.18,19 The risk of developing psychosis in patients with epilepsy is 6 to 12 times higher than in patients without.18 In this case report, the patient developed psychosis after just 2 weeks of topiramate use. The mechanism behind topiramate-induced psychosis has been attributed to its action as a glutamate antagonist at the AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolopropionic acid) and kainate receptors, potentiating gamma-aminobutyric acid (GABA) function. This decreases the functioning of glutamate decarboxylase and converts glutamate to GABA causing a glutamatergic deficient state, leading to psychosis.20 The psychosis during the seizure-free period while on topiramate could be related to seizure control, emphasising the role of forced normalisation or alternative psychosis in such cases. In our patient, it is interesting to note that prior to surgery, the seizures did not abate whilst she was on topiramate but instead she developed psychosis. In this particular case, alternative psychosis cannot be postulated as a reason for psychosis during the time she was on topiramate, and the glutamatergic deficiency theory of topiramate is more likely. After rechallenge with topiramate 2 weeks post-lobectomy, the patient developed no psychosis and remained seizure-free. She only developed psychosis 1 month after her surgery, thus suggesting alternative psychosis in the absence of seizures as the mechanism of psychosis during this phase. It can be seen that psychosis, which developed as a result of topiramate usage, was maintained in the post-lobectomy phase via the mechanism of alternative psychosis.

A large number of patients who suffer from post-lobectomy psychosis have had psychiatric co-morbidity prior to temporal lobectomy, with mood disorder16 and psychosis being the major presentation.21 Thus, co-morbid psychiatric disorders, particularly psychosis, are an important consideration for patients in whom temporal lobectomy is planned as they may lead to an increase
in postoperative psychiatric disorders. Preoperative depression, interictal psychosis, and epileptiform discharges contralateral to the epileptogenic zone are the most frequent predictors of postoperative psychosis. Nonetheless, since AED usage is commonplace in patients with intractable epilepsy and planned lobectomy, psychosis as a result of AED usage could be an important predictor or risk factor for post-lobectomy psychosis.

### Conclusion

As the number of surgical candidates increases and a high incidence of psychiatric co-morbidities is observed, it is important for preoperative planning for temporal lobectomy to take account of these psychiatric co-morbidities. In particular, precautions should be taken when AED-induced psychosis occurs, as this could serve as a predictor of forced normalisation post-lobectomy.

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### References