**A CASE OF *DE NOVO* PSYCHOSIS TEN YEARS FOLLOWING SUCCESSFUL EPILEPSY SURGERY**

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Keywords: Psychosis, temporal lobe epilepsy

The relationship between epilepsy and psychosis has been recognised since the mid-nineteenth century. For pragmatic reasons, psychotic symptoms are always grouped according to their temporal relationship to seizures: ictal, peri/para-ictal and interictal psychoses (IIP). Psychoses without a clear relationship to seizures are usually defined IIP and they usually account for 10–30% of all psychoses of epilepsy in unselected case series with a combined prevalence rate of 5.6% in unselected samples, up to 7.0% when considering only temporal lobe epilepsy.

Temporal lobectomy is an established treatment for patients with intractable epilepsy but ever since the early series, the possibility that surgery may be associated with the occurrence of psychiatric disorders, in particular psychoses, has been discussed. For this reason every epilepsy surgery centre should include neuropsychiatric assessment as part of the presurgical evaluation and postsurgical follow up program. The rate of *de novo* postoperative psychoses is low, but it represents an eminently harmful condition which may affect up to 2% of patients after epilepsy surgery [1]. Whereas mood and anxiety complications typically arise in the early months following surgery, postsurgical psychotic episodes often develop later (i.e. at least six months after surgery), and are independent of seizure outcome. The severity of psychotic symptoms may vary from worried-sceptical mistrusts to paranoid-hallucinatory schizophrenia-like syndromes with increased risk of self-harm behaviours.

We describe a case of *de novo* psychosis ten years after successful epilepsy surgery, in a 55 year-old lady with a previous diagnosis of temporal lobe epilepsy and left sided hippocampal sclerosis. She has a past history of febrile convulsions at the age of 18 months but no other significant antecedent history and normal milestones. She started having focal seizures with loss of consciousness and motor automatisms during childhood and she was diagnosed around the age of four. During the first three decades she presented just with typical temporal lobe seizures preceded by a gastric aura with a frequency of five per year. She was initially treated with carbamazepine and primidone. At the age of 39, she suffered her first secondary generalised tonic clonic seizure, which then continued with a frequency of three per year, together with focal seizures twice a month despite treatment with valproate, phenytoin, clobazam, lamotrigine and levetiracetam in combination with carbamazepine. MRI showed clear left hippocampal sclerosis, and video-telemetry confirmed left temporal onset during typical events. Neuropsychological testing demonstrated weakness in verbal skills and memory that were concordant with the laterality. Pre-surgical neuropsychiatric evaluation identified no prior psychiatric history, no premorbid pathological personality traits and she was considered at low-average risk of psychiatric complications. At the age of 45, she underwent an uncomplicated left amygdalohippocampectomy. Neuropathology of the resected tissue conformed mesial temporal sclerosis. She was subsequently seizure free, withdrew levetiracetam after 1 year, and maintained remission on carbamazepine monotherapy thereafter. However, ten years later, she presented with persecutory delusional ideas related to her new neighbours constantly monitoring her. She also developed visual hallucinations at night time of flickering lights in her home which she believed to be a surveillance mechanism used by her neighbours, and auditory hallucinations of heartbeat noises that accompanied the lights. On mental state examination her appearance was appropriate; she was quite distressed but co-operative. She retained no insight about her delusional ideas and refused antipsychotic treatment or further assessment.

*De novo* psychiatric problems represent a potential complication of epilepsy surgery especially after temporal lobectomy. Two small studies indicated that patients with post-surgical psychosis always have a prior psychiatric history and even those with a claimed *de novo* psychosis had premorbid schizoid or schizotypal personality traits. Our patient is exceptional given her normal pre-morbid psychiatric and personality profile, and a 10 year interval between epilepsy surgery and the psychosis. A recent study comparing patients with hippocampal sclerosis who developed post-surgical psychoses with a matched surgical group without psychosis, reported the onset of psychosis ranging from 2 to 36 months, with a mean of 10.3 months [2]. Most studies have reported seizure and psychosocial outcomes for follow up ranging between 2 and 5 years post-surgery and a few up to 10 years with almost no data about long term prognosis especially regarding psychiatric problems.

Someone may argue that this new onset psychotic disorder is unrelated to the previous epilepsy surgery. Psychotic disorders rarely occur before age 14, but show a typical onset between ages 15–17 up to a maximum of 35 years. Late-onset schizophrenia is usually defined by an onset after age 40 or 45 and seems to represent one fifth of all cases. Patients commonly have visual, olfactory, and tactile hallucinations, and may be more likely to have persecutory and partition delusions [3]. Although it is entirely possible that this patient developed a late-onset schizophrenia it is also evident that the previous epilepsy and subsequent epilepsy surgery represent the only clinically relevant elements in her past history and may represent an element of increased vulnerability.

The underlying pathophysiological mechanisms for psychosis in epilepsy are unclear. Structural and functional neuroimaging studies have implicated left (dominant) temporal lobe pathology with greater reductions in hippocampal volumes, magnetization transfer ratio and single-photon emission computerized tomography (SPECT) perfusion. Proposed mechanisms for the development of psychosis in patients with epilepsy include a ‘kindling’ process where epileptic discharges cause plastic changes in mesolimbic networks and possibly receptor representation, thus affecting brain function. A controversial mechanism to explain how *de novo* psychoses arise in seizure-free patients is termed ‘forced normalisation’, which is defined as the emergence of psychiatric symptoms during periods of significant seizure reduction and accompanied by improvement in EEG activity but this can contribute only to psychotic episodes shortly after surgery. The onset of a psychotic disorder so many years after epilepsy surgery can be in line only with subtle, continuous, changes in brain networks. A number of authors agree that several years, usually 15 years, of active temporal lobe epilepsy are needed in order to develop changes in brain networks which may potentially lead to psychosis [4].

Our case raises a number of possible hypotheses: i) epilepsy-induced changes in brain network leading to an increased risk of psychosis never go away even after successful epilepsy surgery, maintaining an increased risk for psychosis in patients with epilepsy as compared to the general population independent of the prognosis of the epilepsy ; ii) the risk for *de novo* psychosis can remain even after many years from a successful operation and long term follow up is needed and patients informed about this rare possibility.

This single case poses a number of questions rather than answers but definitely highlights the need for long-term follow-up studies of psychiatric complications of epilepsy surgery in addition to neuropsychiatric care as part of any epilepsy surgery centres.

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