Chapter 16

Psychiatric disorders in epilepsy

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Studies have estimated that up to 50% of patients with epilepsy develop psychiatric disorders, the most common being depression, anxiety and psychotic disturbances[1]. These psychiatric disturbances can be classified according to how they relate in time to seizure occurrence, i.e. ictal, peri-ictal (pre-ictal/prodromal, post-ictal) or inter-ictal. Multiple risk factors are associated with the increased risk of psychiatric problems in epilepsy which can be broadly divided into biological (e.g. type and severity of epilepsy), psychosocial and iatrogenic (antiepileptic drugs, surgery).

Ictal

Mood and behavioural changes can occur as direct manifestation of the seizures, including anxiety, depression, hallucinations. The episodes are usually brief (<1–3 minutes), stereotyped, begin and end abruptly, and can be associated with other ictal phenomena (oral, motor automatisms). They usually occur with partial seizures, simple partial (aura) or complex partial seizures but can also occur in generalised seizures.

Ictal anxiety is common, with up to one-third of patients with partial seizures reporting fear as part of their aura, usually in patients with right temporal foci.

Ictal depression occurs less frequently than ictal anxiety and common symptoms are guilt, hopelessness, worthlessness, and suicidal ideation.

Ictal psychotic symptoms can manifest as visual, gustatory or auditory hallucinations and are usually not well defined. They are mainly associated with partial seizures.

Ictal aggression is very rare and mostly involves undirected or unintentional violence.

The treatment of ictal psychiatric disturbances is aimed at adequate seizure control. During an episode, maintaining the patient's safety is the primary concern. Educating patients and their families about the psychiatric manifestations is also important.

Peri-ictal

Pre-ictal or prodromal mood changes usually manifest as irritability, lability, depression, anxiety or aggression and are relieved by the seizure. These symptoms can last a few hours, and sometimes up to a few days before a seizure.

Post-ictal psychiatric disturbances are more likely to occur following clusters of seizures, generalised seizures or status epilepticus.

Post-ictal confusion is characterised by impaired awareness/consciousness and diffuse EEG slowing without ictal discharges. These episodes are usually brief and common after complex

partial or generalised tonic-clonic seizures. Aggressive behaviour may occur and is usually undirected or resistive and the patient is likely to be amnesic for the event.

Post-ictal mood disturbances include depression, anxiety or mania. Post-ictal depression can last longer (up to two weeks) than other post-ictal states. Symptoms range from mild to severe and may involve suicidal behaviour. It has been reported to occur more commonly with right-sided temporal or frontal foci[2]. Post-ictal anxiety symptoms are less common. There are a few case reports of post-ictal mania characterised by symptoms of overactivity, irritability, and disorganised or disinhibited behaviour, which tend to be brief in duration.

Post-ictal psychosis

The prevalence has been estimated to be 6–10% in patients with epilepsy, particularly temporal lobe epilepsy[3]. It typically occurs after a cluster of complex partial seizures (+/- secondary generalisation). There is usually a period of lucidity (12–72 hours) prior to the onset of psychosis. The psychotic symptoms include delusions, hallucinations, thought disorder or mania, which are usually transient but can last several weeks. It has also been reported that some patients with recurrent episodes of post-ictal psychosis may develop an inter-ictal psychosis[4]. Predisposing risk factors are ictal fear, bilateral epileptic foci or gross structural lesions. Mechanisms are unknown but may be related to transient neurochemical changes as a result of seizures, e.g. dopamine hypersensitivity or GABA-related mechanisms.

Treatment of acute post-ictal psychosis may require short courses of benzodiazepines or antipsychotics. Improving seizure control would be the long-term goal.

Inter-ictal

Depression

Research has shown that nearly 40% of patients studied in tertiary epilepsy centres had major depression and therefore it is the commonest psychiatric disorder seen in epilepsy[5]. The true prevalence of depression in epileptic patients in the community has not been established. It is reportedly more common in patients with temporal lobe epilepsy than in generalised epilepsy. The clinical features of major depression include persistent low mood, anhedonia, loss of interest and biological symptoms of sleep or appetite disturbance. However, it is important to recognise that some patients can present with atypical depressive symptoms, referred to as inter-ictal dysphoric disorder[6]. This is characterised by chronic intermittent dysthymia, irritability and anxiety symptoms.

Treatment for depression includes psychological interventions such as counselling, psychotherapy or cognitive/behaviour therapy if appropriate. For moderate to severe depression, antidepressant medications can be prescribed. The potential risk of SSRIs lowering seizure threshold is low (greater risk with tricyclics). Electroconvulsive treatment can be effective for severe medication-resistant depression but there is a small risk of increasing seizures.

Inter-ictal anxiety disorders

The incidence of inter-ictal anxiety disorders is greater than in the general population. Panic disorder, generalised anxiety, agoraphobia, social phobia and obsessive compulsive disorder (rare) can occur. They are reportedly more common in patients with temporal lobe epilepsy, especially with left-sided foci. It is important to exclude other medical causes, e.g. thyroid, endocrine, medication effects, etc. Psychosocial difficulties, social stigma and unpredictable seizures may also contribute to anxiety symptoms.

Inter-ictal bipolar disorder
The prevalence of this is low (<5%) and characterised by periods of depressed mood and episodes of mania. Several case series have reported a preponderance of patients with complex partial epilepsy, particularly with right-sided foci.

Inter-ictal psychosis
The prevalence is reported to be 4–10% in patients with epilepsy, mainly in those with temporal lobe epilepsy[7,8,9]. It is a chronic disorder and clinically resembles chronic schizophrenia (symptoms of delusions, hallucinations, thought disorder) but there are some reports that personality is better preserved. The onset of the psychosis is variable but usually occurs after many years of epilepsy (more than ten years). The risk factors that have been reported are early age of onset of epilepsy, bilateral temporal foci and a refractory course. It has been more commonly associated with left-sided epileptic focus[10,11]. The pathophysiological mechanisms of psychosis in epilepsy are unclear and both focal and generalised brain abnormalities have been implicated[12-15].

Treatment with antipsychotic medications is usually long term. The atypical antipsychotic drugs are potentially less likely to reduce seizure threshold (with the exception of clozapine) or cause extrapyramidal side effects. Lower doses than those used in primary schizophrenia seem to be effective. Psychosocial support and family education are also important.

Treatment-related psychiatric problems

Antiepileptic drugs
Some antiepileptic drugs (AEDs) can cause psychiatric problems, most commonly depression, anxiety, behavioural or cognitive problems and, in rare cases, psychosis. Phenobarbitone, primidone, tiagabine, topiramate, vigabatrin and felbamate have been associated with depression. Psychosis is a rare complication of a number of AEDs such as vigabatrin and topiramate.

Improved seizure control has been associated with the emergence of psychiatric symptoms. Landolt introduced the term ‘forced normalisation’ which refers to a dramatic reduction in epileptiform activity on EEG being associated with the emergence of psychosis or sometimes behavioural/mood disturbances. This phenomenon has been reported with most AEDs and therefore any new drug should be started at low doses and increased slowly. The risk may be higher in patients who are on polytherapy, become seizure free abruptly, or if there is a past psychiatric history.

Epilepsy surgery
Transient mood disturbances (emotional lability, depression and anxiety) have been reported following temporal lobe surgery for epilepsy (about 25%) in the first 6–12 weeks[16]. However, in some patients (10%), symptoms, particularly depression, may persist and require psychiatric treatment. There are also reports of *de novo* inter-ictal psychosis arising after surgery. It is therefore important for pre- and post-surgical psychiatric evaluation to form part of the assessment/management for epilepsy surgery.

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