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Case Report

Neuropsychiatry the Interface between Depression and Epilepsy

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Abstract

The following case study illustrates an interesting case of an elderly patient with chronic mental health problems which include depression, alcohol misuse and anxiety and epilepsy.

This article will illustrate the complexities involved in diagnosing someone with depression and epilepsy and how the two conditions can exist and contribute co-morbidly.

Evidence is presented around the investigations and treatment modalities of this complex area and how psychiatry and neurology can share expertise in the management of these conditions.

Keywords: *Depression; Epilepsy; Anxiety*

Case Summary

A 71 year old lady was referred by her primary care physician to the older person's community mental health team for problems with depression, anxiety and alcoholism. The referral from the primary care physician indicated that she had had a long history of recurrent depression. In the past both she had been treated with numerous antidepressants including mianserin, citalopram, fluoxetine and venlafaxine. More recently she had been treated with cognitive behavioural therapy; however, her depressive symptoms persisted.

She was a retired psychosexual counsellor who had a long and happy marriage to her husband. Her husband had unfortunately developed a Korsakoffs dementia and was in the end stages of his dementia. She herself had been drinking alcohol heavily in the form of red wine. This was quantified as drinking 56 units of alcohol/week. In addition she smoked approximately 30 cigarettes/day.

Her symptoms at the time consisted of depressed mood and anhedonia. There was reduced energy level. There was no suicidal ideation. She had difficulties sleeping, with both initial and middle insomnia. Her appetite was reduced. A mood inventory was taken and she scored 13/15 on the geriatric depression scale (GDS). In addition she complained of very poor memory and short term forgetfulness. A full cognitive inventory was done in the form of an Addenbrookes Cognitive Evaluation (ACE-R) and she scored 96/100. She lost points on fluency and attention. She was at the time reassured that there were no significant problems with her memory, however, that her low mood and anxiety symptoms could be contributing to problems with her memory. She had significant anxiety, and described symptoms of tremor, palpitations, shortness of breath and 'impending doom'. These symptoms would last up to an hour and were present several times per week.

Her medical history was unremarkable and her blood parameters including liver function tests were normal.

On one episode she presented with altered consciousness and weakness in all limbs and was taken to the emergency department. An electrocardiograph (ECG) and magnetic resonance imaging (MRI) scan were done and no abnormalities found.

She was started on treatment for her depression in the form of mirtazepine 30 mg. She was already attending alcoholic anonymous and given further advice to cut down on her alcohol consumption. In addition she was seeing a psychotherapist for counselling whom she had a good relationship with and she continued with that.

Over the course of the next 6 months she managed to cut her alcohol consumption down to 28 units/week. Her mirtazepine was increased to 45 mg. Her mood continued to improve and she scored 12/60 (8-10 borderline abnormal) on the hospital anxiety and depression scale. Her anxiety remained significant and augmenting strategies were discussed with her and she was started on sertraline which was titrated to 100 mg over the course of 2 months. She continued to cut down on her alcohol consumption and was down to approximately 3 units of alcohol per week.

She continued to have altered states of consciousness and presented to the accident and emergency unit on 7 occasions over the next 3 months. Her son had witnessed these events and described his mother as 'catatonic'. There were no other associated symptoms such as tongue biting or incontinence. In-between these episodes she presented normal. I requested a neurology referral. By this time she was abstinent of alcohol. She was assessed and investigated by the neurologist. It was reported that she had altered memory and word finding difficulties. However her Addenbrookes cognitive evaluation mini version (ACE 3) was 30/30. She had potassium gated voltage channel antibodies which were unremarkable. An electroencephalogram (EEG) was requested which demonstrated 'slow wave activity over the temporal lobe'. Following this 24 hour ambulatory EEG was requested she was asymptomatic during the course of this reading, however, during sleep sharp waves were noted more over the left temporal lobe than the right. This was interpreted by neurology as not diagnostic; however, there was a greater liability of partial seizures with this type of activity. She was started on lamotrigine and this was titrated to 75 mg.

Over the course of the next few months her partial seizures resolved completely. She was reviewed in clinic; she was euthymic and functioning well, without any anxiety with a GDS of 3/15. She rated herself as being back to normal.

Discussion

This case illustrates well the complexity of neuropsychiatric presentations. In this case an elderly lady who has a history of recurrent depression, harmful alcohol use, and new onset partial seizures. The unusual aspects of this case include the presentation of partial seizures after the depression.

Aetiology

It is well recognised that depression is a common in patients with epilepsy. Indeed depression is the most common psychiatric disorder in patients with epilepsy with estimates at around 38 - 43% [1].

However there is also data to suggest that there is bidirectionality in the presentation of epilepsy in patients with depression. Three population-based control studies indicate that people with a history of depression have a 4- to 7-fold higher risk of developing epilepsy [2]. In one of these studies, a prior history of suicidality was associated with a 5-fold increased risk of developing epilepsy [3]. The bidirectional relationship does not imply causality but rather suggests that common pathogenic mechanisms are operant in both conditions, with the presence of one disorder contributing to the development of the other.

It is also recognised that there is a pleomorphic presentation of depression in patients with epilepsy including irritability, anxiety and poor frustration tolerance, a waxing and waning course, with interspersed symptom free periods of one to several days. Depression has been identified more frequently in patients with seizures of frontal and temporal lobe origin. That is seizures involving the limbic circuit.

The association is greater than for patients with generalised seizures [4]. Additional structural changes have been associated with both depression and epilepsy; these include atrophy of temporal and frontal lobe structures [5] (identified by high resolution MRI and volumetric changes) in the amygdala, hippocampus, entorhinal cortex, temporal lateral neocortex, as well as in the prefrontal, orbitofrontal, and mesial frontal cortex, and to a lesser degree of the thalamic nuclei and basal ganglia.

Diagnostic Challenges

Kanner., *et al*. [6] described how these patients are difficult to place into a discrete diagnostic category. Their symptoms can be extreme at the one end of the spectrum with anhedonia, and at the other end they can have recurrent intermittent periods of symptom free period. This means that the patient's symptoms fluctuate between a major depressive episode and a more chronic dysthymia picture. To make things even more complex, peri-ictal symptoms are often associated with dysphoric mood changes that can be preceded by an absence of any psychiatric symptoms.

It is however, useful in a psychiatric or neurology clinic to have in ones mind key symptoms to help detect and treat depression. A history of anhedonia and a depression rating scale such as the Hospital Anxiety and Depression Scale (HADS) or Geriatric Depression Scale (GDS) are useful tools in the detection of co-morbid depression. However, a careful and methodical history will invariably give a more complete picture.

Treatment

There is surprisingly little in the literature about treatment of depression and epilepsy. A systematic review [7] in 2014 concluding that there was a statistically significant effect of venlafaxine on depressive symptoms in patients with epilepsy. However, the authors concluded that there was insufficient evidence to give a recommendation on the class of antidepressant drug or the dosage for patients with depression and epilepsy. In addition the lack of data meant there was insufficient evidence to support psychotherapy or other treatment modalities in patients who were unable to tolerate antidepressants due to side effects.

The literature suggests that psychiatrists and neurologists are reluctant to start antidepressants in patients with epilepsy because of the theoretical risk of lowering the seizure threshold in patients. However, it is uncertain whether combined treatment with antiepileptic drugs is protective against seizures in patients with depression and epilepsy. Drugs such as buproprion, maprotiline, and amoxapine with the strongest proconvulsant effects should be avoided in patients with epilepsy [4].

Given the limited amount of evidence around the treatment options in this subgroup of patients, it is of little surprise that there are many unanswered questions. There is uncertainty as to whether a depression can be treated with a mood stabilising drug with antiepileptic properties such as lamotrogine, carbamazepine or valproate alone. The corollary of this is could a depressive episode be triggered by the discontinuation of one of these drugs.

It is known that antiepileptic drugs are efficacious in treatment and remission of patients with bipolar affective disorder, which raises the question of whether there is a similar pathophysiological process in patients with major affective disorders and patients with epilepsy. The common pathways and neuroanatomical circuits which involve the limbic system including temporal lobes and subcortical structures would suggest that the two conditions are linked.

In addition because of this close association, there could be a common pathway in treatment modalities including mood stabilising drugs for both depression and epilepsy.

Another consideration is the interactions that antiepileptic drugs (AEDs) and antidepressants have on each other. Some AEDs including carbamazepine and phenytoin are enzyme inducers and can significantly lower the blood plasma levels of antidepressants. Phenytoin is also known to have depressive effects and is probably best avoided when treating depression and epilepsy.

Some antidepressants including fluoxetine, paroxetine and to a lesser extent sertraline inhibit the cytochrome P450 liver enzymes and therefore reduce the metabolism of AEDs.

Prognosis

Undetected depression and anxiety symptoms in patients with epilepsy significantly increase the general morbidity and health costs associated with this subgroup. The risks of suicide by about 5 times in patients with epilepsy compared to the general population [8]. There is an association with worsening quality of life scores [9,10] and a significantly increased cost to medical services with increased use of medical resources. Therefore appropriate detection and treatment can significantly reduce the burden to both the patient and the wider health economy. The association between epilepsy and depression and of untimely death has been chronicled in famous musicians and artists. Both Ian Curtis of the band Joy Division and Vincent Van Gogh ended their own lives whilst battling with symptoms of both depression and epilepsy.

Conclusion

In summary both the detection of depression and epilepsy and its treatment is a complex area. It requires a careful and systemic approach requiring close collaboration with both neurology and psychiatry to ensure that the patient gets the most appropriate treatment. It requires careful thought and a good awareness of the pharmacology of the agents used. I would argue that given how common these conditions are, there is a lack of research. Further research is required to explore whether there is a common pathway to major affective disorders and epilepsy and treatment modalities.

However, early detection of both depression and epilepsy can improve the quality of life and lower the burden of cost to the wider health economy. This may indeed require close collaboration and a good working interface between neurology and psychiatry and for the disciplines to support each other in the management of this complex condition.

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