

Anxiety Disorder Due to Epilepsy: A Case Report



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SUMMARY

Epileptic patients present with psychiatric disorders more frequently than the general population and patients with other chronic medical conditions. Psychiatric disorders can co-occur with epilepsy and can be caused by epilepsy. Personality changes, as well as psychosis, and mood or anxiety disorders can occur in association with epilepsy. Anxiety disorders due to epilepsy can manifest as generalized anxiety disorder, panic disorder, phobias, or obsessive-compulsive disorder. The risk of an anxiety disorder is higher in patients with focal epilepsy, especially those with temporal lobe epilepsy, but an anxiety disorder can also occur in patients with frontal lobe epilepsy or generalized tonic-clonic epilepsy. Herein we present a 41-year-old female patient with comorbid anxiety disorder and epilepsy that improved following initiation of antiepileptic medication.

The patient's EEG showed abnormalities, particularly in the frontal lobe. Epileptic activation-associated anxiety disorder presented as phobia of swallowing and the patient exhibited features of generalized anxiety disorder. Following initiation of antiepileptic medication, the seizures stopped and the symptoms of anxiety disappeared in two weeks. The patient was receiving psychotherapy once every 2 weeks. The patient remained asymptomatic during 2-years of follow-up. This case highlights the importance of differential diagnosis of underlying epilepsy in patients with acute severe anxiety and the efficacy of proper medical treatment, which was given in the presented case for the underlying pathology of anxiety.

Keywords: Epilepsy, anxiety disorder, anticonvulsants

INTRODUCTION

It was reported that the frequency of comorbid psychiatric diseases in epilepsy patients varies, as follows: anxiety disorders: 23%-39%; major depression: 16%-20%; dysthymia: 8%; other psychiatric disorders: 9%. Research has shown that anxiety disorders are more common in female epilepsy patients and are associated with the frequency of seizures, whereas depression is not related to trauma or the frequency of seizures (Desai et al. 2010; Phabphal et al. 2007). It was reported that patient age, seizure type, marital status, duration of disease, employment status, level of educational, use of drugs, and socioeconomic status were not predictors of comorbid anxiety disorder or depression (Phabphal et al. 2007).

Obsessive-compulsive symptoms, common anxiety symptoms, panic seizures, and panic disorder are more frequently observed in epileptic patients than in healthy controls. The risk of an anxiety disorder is higher in cases of focal epilepsies than other cases (especially temporal lob focused), whereas anxiety disorders occur in those with frontal lob epilepsies and generalized epilepsies (Beyenburg et al. 2005). The severity of seizures and right temporal focus might be associated with anxiety in epileptic patients that are resistant to treatment (Scicutella 2001). The amygdala plays an important role in the formation of temporal-derived anxiety symptoms and epileptic discharges. Ictal fear was noted in about 50% of epileptic patients with amygdala atrophy on the same side

Received: 04.11.2012 - Accepted: 28.07.2013

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as seizure focus, and amygdala volume was lower in patients with temporal lobe epilepsy and ictal symptoms of anxiety (Beyenburg et al. 2005); however, there is no consensus on the relationship between the frequency of seizures and lateralization of focus, and anxiety (Scicutella 2001). It was suggested that anxiety in some epilepsy patients could be related to the recurrence of seizures and the fear of losing control, and that the frequency of seizures could be related to patient perception of hazard (falling down, dying) (Beyenburg et al. 2005).

Herein we report an epilepsy patient that presented due to common symptoms of anxiety disorder and inability to swallow. Drug therapy was initiated in accordance with the symptoms; the patient had generalized tonic clonic style seizures on d 5 of drug therapy and the symptoms of anxiety resolved following anticonvulsant therapy.

Case

The patient was a female teacher that was born in 1971 and had a 10-year-old daughter. She presented to Dokuz Eylül University, School of Medicine, Psychiatry Polyclinic in May 2010 with complaints of inability to swallow solid food, the sensation of stickiness in her throat, and belching. These complaints began in December 2009 after her husband (at the time) that had been living in a separate residence for 5 years, though they met every month and had a close relationship³including sexual, filed for divorce. She experienced a bitter taste in her mouth after eating bread, rice, and bakery products. She presented to the department of internal diseases in January, 2010 and as her symptoms could not be explained medically she was referred to the department of psychiatry, but she did not present.

The patient had presented to Dokuz Eylül University, School of Medicine, Psychiatry Polyclinic in 2004 with sadness and anhedonia symptoms when her husband thought about divorce for the first time; sertraline treatment was planned, but she did not return to the department and did not use the drug. She reported that she did not need to visit the department of psychiatry during this time because she did not have any psychiatric complaints. Due to an increase in anxiety and sadness as comparing symptoms in December 2009, that was noted during a psychiatric assessment in March 2010 (after divorce proceedings began), the patient was prescribed mirtazapine in consideration that she was having a major depressive episode, but she did not use the medication. She subsequently presented to the emergency department twice during the following 3 months due to the sensation of stickiness in her throat; an organic etiology was ruled out and she was referred again to the department of psychiatry. At the psychiatry unit of the university to which she presented in June 2010 due to an inability to swallow solid foods, the sensation of stickiness in her throat and belching an atypical and psychotic major depressive episode was suspected; she was hospitalized and examinations were performed in relation to her complaint of inability to swallow. The patient declined upper gastrointestinal

system (GIS) endoscopy. Cranial MRI findings were normal. EEG showed active generalized epileptiform discharges. The patient was discharged from the hospital after 3 d because she wanted to return to work. The patient declined outpatient following-up by the neurology department.

The patient presented to Dokuz Eylül University, School of Medicine, Psychiatry Polyclinic with the same complaints about 15 d after discharge, and was hospitalized for differential diagnosis and therapeutic purposes. During psychiatric observation while hospitalized she was conscious and cooperative, she was oriented to place, time, and person, her mood and affect were depressive and anxious, her memory was normal, she had impaired attention, her judgment, abstract thinking, and reality testing were appropriate, and she described the feeling of bad taste in perception. The patient reported worrying that she would not recover, would lose her daughter, and that she was worthless. The patient exhibited psychomotor agitation, but her sleep and libido were normal. Her food intake decreased due to difficulty swallowing and she lost 7 kg over the course of 2 months. Her physical and neurological findings were normal. Her hematological and biochemical findings were also within normal limits.

The patient's Hamilton Depression Rating Scale (HAM-D 17) score was 17 and Hamilton Anxiety Rating Scale (HAM-A) score was 29 in first week of hospitalization she reported that she could not eat solid food, that even liquids got stuck in her throat, and that she could not swallow; she feared to live the feeling of the bitter taste again. She was associated with a possible poisoning; however, this consideration was not delusional. In inpatient unit the patient constantly had the request to interview in intense worry. She requested to be discharged because her condition was not similar to those of the other patients in the ward in the first days of hospitalization. She had difficulty obeying the hospital rules and she argued with the nurses about the rules. She refused to eat hospital food, and wanted her mother to cook and bring liquid foods for her; she had difficulty separating from her mother. A series of consultations and examinations were planned for the purpose of excluding any possible medical causes for her symptoms.

The patient was referred to the department of otorhinolaryngology, but she refused to undergo endoscopic examination. She was fearful of the side effects psychiatric and other drugs and examinations, such as endoscopy. She feared that something bad would happen to her and that her daughter would be left alone. She could participate in psychiatric interviews for only five or ten minutes due to her anxiety, which persisted all day. With the pre-diagnosis of anxiety disorder not otherwise specified, escitalopram drops 5 mg d⁻¹ was started on d 4 of hospitalization and 5 d later was increased to 10 mg d⁻¹. She took lorazepam 1 mg whenever deemed necessary based on her anxiety, but the total dose did not exceed 3 mg d⁻¹. The patient's HAM-A score was 31 on d 9 of hospitalization. The patient and family histories were negative for mental and neurological diseases, but the patient's mother

was described as a worrier. The patient did not report any mental or physical disease, except for major depression, which was diagnosed in 2004.

The day escitalopram was increased to 10 mg d⁻¹ the patient had a generalized tonic clonic seizure that lasted nearly 2 min; therefore, valproic acid solution 1000 mg d⁻¹ was started and escitalopram was discontinued. The patient's anxiety was much more severe on the day she had a seizure, as compared to earlier. The EEG findings obtained when she was first hospitalized in June 2010 that were indicative of active generalized epileptiform discharges were re-assessed. It was determined that the ground rhythm was well developed and arranged, she had alpha rhythm reactive to eye opening and defined as short-duration generalized spike-wave discharges with higher amplitudes in the frontal regions with frequent intervals along the trace, which were considered to be indicative of frontal based seizure. The patient did not have any other seizures and the patient's anxiety decreased markedly 1 week after starting valproate; her HAM-A score decreased to 19. The patient was then able to eat all solid foods. The patient's reported experience of a bitter taste in the mouth was considered a seizure-related phenomenon. She was able to control her anxiety and follow the hospital's rules and she was able to make interviews in usual length. Her HAM-A score decreased to 11 on the 35th d of hospitalization. The valproic acid dosage was set so that the patient's serum valproic acid level was 80-100 µg mL⁻¹ while hospitalized.

She was discharged four weeks after seizure and valproic acid 750 mg d⁻¹ was continued post discharge. The patient did not have any epileptic seizures or symptoms of anxiety during a 2-year follow-up, during which time her divorce procedures continued. The patient was interviewed every 2 weeks, during which her work, social, and private lives were assessed. She was able to meet her ex-husband and together evaluate their daughter's needs and share responsibility for her care.

Discussion

All symptoms of severe anxiety and phobic avoidance that resulted in the present patient's hospitalization were completely resolved using antiepileptic treatment, which shows that the table is associated with epileptic symptom. In particular, the presented patient's experience of a bad taste in her mouth is characteristic of very rarely encountered gustatory aura (Chen et al. 2003). The sensation of a metallic taste is the most commonly described symptom of such seizures, which can be experienced as pleasing or disgusting taste hallucinations (Acharya et al. 1998). Anxiety in association with epilepsy has several forms. One form is peri-ictal anxiety, which occurs before an epileptic seizure or during the days following the end of a seizure. Anxiety can occur seconds or minutes before a complex partial seizure, and can be stereotypic. Anxiety can also occur more than a few minutes before a seizure and may not be stereotypic. This situation is generally characterized by irritability, emotional lability, depressive symptoms, and

aggressiveness (Beyenburg et al. 2005). Immediately following the end of a postictal anxiety attack there is often clouding of consciousness and it is usually associated with postictal dysphoria and depression. Rarely, anxiety can also occur in isolation. Fear can also accompany anxiety, lasting for hours-days during the postictal period (Scicutella 2001).

Another form of epilepsy-associated anxiety is ictal anxiety. The sense of fear is a part of the seizure. Patients' descriptions of fear vary from a feeling of tension to an intense sense of fear and panic. Ictal anxiety usually lasts a 2-3 s-2 min. Fear can occur as the only symptom of a simple partial seizure different from other ictal phenomena, and it can also be the aura of a complex partial seizure (Scicutella 2001). There may be autonomic symptoms associated with fear during a simple partial seizure, such as palpitation, epigastric disorder, nausea, and increase in breathing rate, paleness or flushing. Hallucinations, déjà vu, and jamais vu experiences, and depersonalization and derealization can also be observed. Amnesia can develop versus anxiety when the seizure transforms into a complex partial seizure. Ictal anxiety is most often noted in those with temporal epilepsy (5%-20%). Some cases with complex partial status epilepticus, which can last 12 h-3 months in the form of a sense of fear, were also reported; symptoms of anxiety disappeared in these cases following right temporal lobectomy (McLachlan & Blume 1980; Henriksen 1973). Ictal anxiety disorders severely complicate the differential psychiatric diagnosis. A structural lesion was observed in the right temporal lobe in 5 epileptic patients that were erroneously diagnosed as panic attack (Sazgar et al. 2003); however, patients with panic disorder can also be misdiagnosed as epilepsy.

Lastly, symptoms of anxiety can occur during the interictal period in epilepsy patients. The symptoms of anxiety might occur as a result of adaptation to epileptic seizures, the fear of having a seizure, and the side effects of anti-epileptic drugs or surgical treatment of epilepsy. Interictal anxiety is not a direct consequence of epileptic seizures and is often noted in patients with limbic system epilepsy (Beyenburg et al. 2005). The frequency of interictal anxiety disorder was reported to be 10%-66% by in hospital-based and outpatient-based epilepsy studies (Scicutella 2001).

Anxiety and agitation were for more severe in the presented patient the day she had an epileptic seizure than earlier during her hospitalization. She had severe anxiety, which lasted in 1 hour after having a seizure. She was obviously irritable, but not aggressive. Clouding of consciousness did not accompany the table. It was considered that the patient's anxiety table as characteristic of peri-ictal anxiety, based on ongoing seizures because of the epileptic activity noted via EEG nearly 1 month earlier. The frequency of anxiety disorders in treatment-resistant epileptic patients scheduled for surgical treatment is 10%-44%, versus 11% in primary care epileptic patients (Koch-Stoecker 2002; Trimble & Schmitz 2002). Generalized anxiety disorder (GAD) is most frequently observed in epileptic patients. It is thought that GAD usually

develops in association with psychosocial difficulties related to having a chronic disease and the unpredictable course of epilepsy (Özmen & Tecer 2008). It was reported that the frequency of panic attacks was 6-fold higher in patients diagnosed with epilepsy than in controls, and that the panic attack point prevalence was 15%-30% (Beyenburg et al. 2005). Panic disorder progress with panic attacks so paroxysmal symptoms may be confused with epileptic seizures and may not be defined. Fear is frequently encountered in patients with partial seizures originating in the temporal lobe and is sometimes difficult to differentiate from panic attacks. Fear is frequently encountered (10%) relative to its symptoms during aura associated with temporal lobe attacks (Taylor & Lochery 1987). Panic attack is the only anxiety symptom that can be directly produced by the seizure among all anxiety disorders. Phobic disorders are also common in epilepsy. The most frequently observed phobias are fear of having seizures, which leads to agoraphobia or the fear of having an accident outside the house, and fear of social embarrassment, which leads to social phobia (Beyenburg et al. 2005). Phobias are more frequent in patients with seizures that cannot be controlled. Obsessive-compulsive disorder (OCD) can occur during several phases of a seizure. Obsessions can be a part of epileptic aura, even if it can be seen a little in temporal lobe epilepsy (Beyenburg et al. 2005). Cases of OCD occurring for the first time following surgical treatment of epilepsy have been reported (Kulaksızoğlu et al. 2004). It was reported that OCD developed during the first week following the use of topiramate (Özkara et al. 2005). In the present case the anxiety table had developed due to epileptic activity conforms to a GAD table, which is characterized by phobia and multiple worries that emerge in the form of fear of swallowing descriptively. Additionally, health anxiety was also a part of the clinic table.

If an anxiety disorder accompanying epilepsy is left untreated the frequency of the seizures may increase. The first step in the treatment of anxiety in epileptic patients is providing information and support. While some anti-epileptic medications increase anxiety, some decrease it. It was reported that anti-epileptics with a dominant glutamatergic effect lead to activation of neurons and cause weight loss and an increase in the severity of anxiety, and that anti-epileptic medications that increase GABAergic activity cause sedation, cognitive impairment, weight gain, and a decrease in the severity of anxiety. Vigabatrin, tiagabine, gabapentin, pregabalin, and valproate are effective in the treatment of anxiety disorders (Beyenburg et al. 2005). Epileptic seizures and associated symptoms of anxiety fully resolved in response to valproate treatment in the presented case.

The first pharmacotherapy option for the treatment of anxiety disorders in epileptic patients is serotonin reuptake inhibitors (SRIs), because of their side effect profiles; they less frequently cause medication-medication interactions and have fewer effects on neuronal stimulation, and thus are less likely to trigger seizures (Beyenburg et al. 2005; Jackson & Turkington

2005; Scicutella 2001). Nonetheless, anxiety did not decrease in the presented patient in response to SRI treatment; rather a seizure occurred after increasing the dosage. Because she complained of a bad taste in her mouth before SRI treatment started, the seizure was not considered to be related to the medication; it was thought that ongoing seizures transformed into generalized tonic clonic seizures. The marked decrease in the severity of the patient's anxiety after having a seizure further indicated that the seizure was not associated with the SRI. Clinicians should be aware that long-term use of benzodiazepines is associated with the risk of addiction, even though they have both anxiolytic and antiepileptic effects (Beyenburg et al. 2005; Scicutella 2001). Perhaps if the EEG findings obtained during the presented patient's first hospitalization were neurologically assessed in a timely fashion drug therapy would have started sooner and her anxiety would have resolved before having a generalized tonic clonic seizure. As such, clinicians must be aware that epilepsy patients, primarily those with temporal- and frontal-based epilepsies, may develop symptoms of anxiety; therefore, accurate differential diagnosis is important for initiating the correct treatment and limiting the occurrence of medication interactions.

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