



## Case Report

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# Herpetic Encephalitis Sequelae Can Be Traumatic: A Case Report

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### Abstract

Herpes Simplex Encephalitis often have significant short-term and long-term neurologic and neuropsychiatric morbidities. There is limited information when evaluating patients with post encephalitic sequelae and their increased risk of falls due to motor deficits and therefore, the risk of developing a 'fear of falling' manifesting as PTSD. Here we describe a patient with post- encephalitic motor, neurologic and neuropsychiatric sequela who presents with depression and PTSD with panic attacks following multiple falls which posed perceived life-threatening events in a repeated matter. Furthermore, we review the neuroanatomical predispositions of developing PTSD in patients with HSE and the controversy of the definition of 'trauma' as per different DSM editions. It is important as physicians to understand that what is pathological about PTSD is defined not by the nature, but by the persistence and severity of its symptoms. We must look at the patient as a whole and evaluate what risk factors can predispose to certain diagnosis and what can be perceived as traumatic to increase detection and provide appropriate treatment. The prompt recognition and treatment have important implications for patient quality of life.

### Introduction

Viral encephalitis is a condition in which a virus infects the brain and produces an inflammatory response, with Herpes Simplex Virus-1 being one of the most common. Herpes Simplex Encephalitis is a potentially life-threatening condition, with a mortality rate of 60% to 70% in people with untreated illness. Those who survive often have significant short-term and long-term neurologic and neuropsychiatric morbidity [1].

Neurological sequelae for these patients can be associated with risk factors for falls, such as gait and balance disorders, deficits of lower extremity strength, sensation, and coordination, in addition to cognitive impairments. Falling has behavioral and psychological consequences in the immediate and long- term period after the experience. These include decreased activity and raised levels of anxiety and depression [2].

Chung et al., (2009) were the first to hypothesize that a fall can be an event that may lead to the development of Post-Traumatic Stress Disorder (PTSD). The 'Fear of falling' syndrome, presented as a specific consequence of a fall, corresponds to the association of

postural motor symptoms with several behavioral symptoms such as anxiety. They suggested that some patients thought to have 'fear of falling' may be manifesting PTSD and require identification to enable therapeutic intervention [3].

There is limited information when evaluating patients with post encephalitic sequelae, their increased risk of falls and therefore, the risk of developing PTSD. Furthermore, for patients with encephalitic sequelae, it is difficult to discern between psychiatric symptoms that stem from an organic cause and those that stem from a psychogenic one. Due to the overlapping nature of neurologic and psychiatric symptoms, many can be overlooked. Therefore, increased awareness among physicians of PTSD and panic attacks as a possible outcome of Herpetic Encephalitis and the neurological impairments that follow, can help to increase the likelihood of their detection and treatment.

### Case Report

#### Clinical Presentation

Mrs. R is a 42-year-old female who had presented to an emergency room 6 years earlier with symptoms such as headache, fever, disorientation, and seizure-like activity. It was at this time that she was diagnosed with Herpetic Encephalitis HSV-1, she was admitted and received inpatient treatment for 21 days. Inpatient MRI with and without contrast results included findings such as: "Examination shows bilateral restricted diffusion along the right and left hippocampi and abnormal signal intensity involving bilateral frontal and mesial temporal lobe regions".

In the months following discharge, the patient required occupational and physical therapy due to residual right sided hemiparesis. Further evaluation by Neuropsychological testing confirmed Mrs. R also now suffered of Mild Cognitive Impairment. The sequela of these symptoms created an impact in her daily living, and she developed depressive symptoms such as sadness, poor concentration, loss of interest, hypersomnia, low self-worth, and anxiety for which she began psychiatric treatment with Sertraline and Clonazepam.

However, as years have passed, Mrs. R has suffered multiple falls due to the right sided hemiparesis. Since falls started to become more frequent, the patient began to present episodes described as palpitations, trembling, shortness of breath, feeling dizzy, tingling sensation in four extremities and fear of losing control. These would happen initially when patient was to go up or down any stairs, had to stand or sit from a chair or get in or out of a vehicle. However, the episodes became more frequent and unexpected, they would sometimes happen out of the blue. Mrs. R sought further neurology evaluations to rule out possible residual seizure-like activity, however negative EEG discarded this possibility. She did not present other worries unrelated to her falls.

Mrs. R began to fear for her life during these falls and became hyper vigilant, exaggerated startle, experiencing flashbacks of previous falls whenever confronted with a situation that would represent a risk (stairs, walking a distance, crossing the street, getting in and out of chairs/bed/vehicle, etc...), she would awaken at night having experienced nightmares of falls. She began to avoid certain

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areas or activities that she associated as a fall risk and began to present isolation, as well as diminished interest or participation in significant activities. Whenever in public she fears the event of a panic-like symptom or fear of falling, perceived as an embarrassing event, and thus avoids them. She denied suicidal ideation, homicidal ideation, delusions, or perceptual disturbances. She denies obsessions or compulsions. She does not present a history of traumatic experiences except for exposures to natural disasters.

Mrs. R is a retired substitute teacher; she does however continue providing private tutoring for elementary school children. She lives in Caguas, a small rural town in Puerto Rico with her husband and her 17 y/o daughter whom she identifies as major support. She does not smoke, drink alcohol, or use illicit drugs.

Mrs. R has no psychiatric history before encephalitis and there is no known family history of psychiatric illness.

Review of systems is negative except for as mentioned above.

### **Mental Status Exam (at present time)**

Mental status exam reveals that Mrs. R is dressed in casual street clothes. She is cooperative throughout interview. Her speech is mildly accelerated and normal tone. Her mood appears anxious and preoccupied. Her affect is mood congruent with anxiety. She is not suicidal or homicidal and does not present delusions. She is preoccupied of experiencing recurrent panic attacks as well as of performing certain activities alone. She speaks spontaneously and has goal-oriented speech. She has not hallucinated, only during panic episodes does she experience feelings of depersonalization. She is alert and oriented to time, place, and person. She has good insight and agrees that she may have symptoms of post-traumatic stress disorder with panic attacks and agoraphobia. She has good judgement.

### **Evaluation**

Mrs. R experienced herpetic encephalitis, as an aftermath of this event she has experienced multiple falls which posed perceived life-threatening events in a repeated matter. Although her symptoms clearly present panic attacks and can fit the criteria of panic disorder, she has developed additional symptoms that are beyond that diagnostic presentation. Having exposure to these traumatic events she has developed symptoms that include: 'Flashbacks' and physiological reactions whenever exposed to internal or external cues of fall events, blames herself about the causes of these frequent falls, has persistent negative emotional state such as fear and anger, she has diminished interest and actively avoids certain activities and presents hypervigilance in her surroundings due to fear of falling with exaggerated startle response. Taken together these symptoms meet the criteria of post-traumatic stress disorder [4]. In fact, upon further evaluation of the symptoms with the PTSD Checklist-Civilian Version, she scored a total of 57. This score is indeed suggestive of the presence of PTSD diagnosis.

Furthermore, Mrs. R presents many symptoms that fit the criteria for panic attacks. She experiences episodes of abrupt onset and escalating palpitations, trembling, shortness of breath, feeling dizzy, tingling sensation in four extremities and intense fear of losing control. Beck Anxiety Inventory scored a total of 27 which indicates moderate anxiety. For the diagnosis of depression, Mrs. R felt sadness, depressed, poor energy, low self-esteem, lack of interest and poor concentration. This coupled with Patient Health Questionnaire-9 score of 12 are consistent with Major Depressive Disorder, Moderate.

As it often happens when there is a diagnosis of PTSD, it is difficult to discern if these mood symptoms are a manifestation of post-traumatic etiology or a comorbid condition.

It is important to note that individuals with PTSD are 80% more likely than those without PTSD to have symptoms that meet diagnostic criteria for at least one other mental disorder (e.g., depressive, bipolar, anxiety, or substance use disorders) (4). PTSD is more prevalent among females than among males and tend to experience PTSD for a longer duration than do males. (4) Finally, there is considerable comorbidity between PTSD and major neurocognitive disorder and some overlapping symptoms between these disorders (4). This is important as Mrs. R presented with neurocognitive disorder as a sequela of herpetic encephalitis and may be overlapping.

Patient began treatment with selective serotonin reuptake inhibitor, Sertraline, currently on 200mg daily, as well as benzodiazepine, Clonazepam 0.5mg twice daily. There has been improvement in mood, depressive symptoms and in frequency of panic attacks however patient persists with constant fear of falling and symptoms of PTSD such as 'Flashbacks', feelings of guilt about falls and hyper vigilance in her surroundings.

Even further, Mrs. R faces social difficulties that have limited her improvement. Due to her low socioeconomic status, she lacks transportation, has limited social support and poor access to medical treatment. She has not been able to receive proper physical therapy and lacks proper medical equipment to support her activities of daily living.

### **Discussion**

Herpes Simplex Virus-1 (HSV-1) is amongst the most common causes of viral encephalitis (1). Infection of HSV-1 occurs after reactivation from its reservoir– the trigeminal ganglion and spreads into the frontal and temporal lobes [5]. The fronto-orbital region, temporal lobes, hippocampus, cingulate gyrus and insular cortex are the most affected areas. In these sites brain edema followed by haemorrhagic necrosis leads to the cytolysis of neurons, astrocytes and oligodendrocyte. Neuroimaging studies have proven that there is a specific HSV affinity to the limbic cortex. The location of the inflammatory and necrotic changes explains the behavioural, emotional and personality disorders commonly occurring during HSV-1 encephalitis both acutely and residually [6].

The emotional-processing and fear response have been historically linked to the brain structures referred to as the limbic system. The limbic system includes the hippocampal formation, amygdala, septal nuclei, cingulate cortex, entorhinal cortex, perirhinal cortex, and parahippocampal cortex [7]. The hippocampus has direct connections to the amygdala as well as other structures of the limbic system. Thus, all these areas can be influenced by the hippocampus [7]. This is important to note in Mrs. R's case as MRI imaging during infection showed involvement of bilateral hippocampi.

One of the most extensive research done in the field of neuroimaging in anxiety disorders has been conducted on PTSD. Functional neuroimaging studies have recurrently demonstrated amygdalar hyperactivity and hypoactivity in the hippocampi in PTSD [8]. In current models of PTSD, amygdala hyperactivity reflects the persistently elevated fear response, and hypo activity in the hippocampus, whose function it is to provide information about the context of a situation, might be attributable to difficulties in identifying safe contexts. However, studies indicate that some of the

observed abnormalities, like reduced hippocampal volume, can be a predisposing factor for the development of PTSD on the one hand, but also be a consequence of the disorder and show a further decrease over time [8].

Given these findings, there is a possibility that, because of HSV-1 encephalitis, necrotic changes could have occurred post bilateral hippocampi inflammation seen in Mrs. R's neuroimaging during acute infection. In turn, hypoactivity of hippocampal formation has predisposed Mrs. R to develop anxiety disorders, with a particular vulnerability to PTSD.

However, on a psychological aspect, the diagnosis of PTSD remains a controversial topic, specifically as to what constitutes Criterion A on DSM-V, the issue involving the question of how broadly or narrowly 'trauma' should be defined. Criterion A has had several modifications throughout the years. The original concept of PTSD as a response to an event "generally outside the range of usual human experience" was broadened when it was realized that the prevalence of traumatic events was higher than had been supposed. The definition of a traumatic stressor has further broadened in that a person who is not personally and directly exposed to trauma but rather learns about someone else being exposed [9]. The non-Criterion A events that have been reported to produce PTSD symptoms are: marital disruption, affairs, and divorce among others [10]. Specifically, some studies support the idea that patients with multiple falls who develop a 'fear of falling' might reflect underlying PTSD (3). It has also been shown that those who have genetic, epigenetic, or neurobiological vulnerabilities may in fact experience PTSD to trauma of lower intensity [9].

Thus, given the neuroanatomic vulnerabilities of Mrs. R in combination with her perceived traumatic experience of multiple falls and the symptomatology that pursued can predispose her to a PTSD diagnosis. In the case of Mrs. R, the consideration of PTSD as a diagnosis has been essential for the development of a treatment

plan. She has shown improvements in mood symptoms but has continued with hyper arousal and avoidance symptoms which have required to be addressed. It is important as physicians to understand that what is pathological about PTSD is defined not by the nature, but by the persistence and severity of its symptoms. We must look at the patient as a whole and evaluate what risk factors can predispose to certain diagnosis and what can be perceived as traumatic to increase detection and provide appropriate treatment.

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