

LESSONS LEARNED AT THE
INTERFACE OF MEDICINE AND
PSYCHIATRY

The Psychiatric Consultation Service at Massachusetts General Hospital (MGH) sees medical and surgical inpatients with comorbid psychiatric symptoms and conditions. Such consultations require the integration of medical and psychiatric knowledge. During their thrice-weekly rounds, Dr. Huffman and Dr. Stern discuss the diagnosis and management of conditions confronted. These discussions have given rise to rounds reports that will prove useful for clinicians practicing at the interface of medicine and psychiatry.

Dr. Huffman is Chief Resident at MGH and a Clinical Fellow in Psychiatry at Harvard Medical School. Dr. Stern is Chief of the Psychiatric Consultation Service at MGH and an Associate Professor of Psychiatry at Harvard Medical School.

Corresponding author:
Jeff C. Huffman, M.D.
(e-mail: Jhuffman@partners.org).

Poststroke Neuropsychiatric Symptoms and Pseudoseizures: A Discussion

Jeff C. Huffman, M.D., and Theodore A. Stern, M.D.

Is it reasonable to assume that just about everyone becomes depressed following a stroke? Which neuropsychiatric manifestations are most readily confused with the signs and symptoms of depression? How can one determine whether unusual convulsive symptoms are manifestations of true seizure activity or psychogenic episodes?

Neuropsychiatric sequelae of cerebrovascular accidents (CVAs) are common and varied. The presented case highlights aspects of the neuropsychiatric evaluation of a poststroke patient with mood symptoms and unusual seizure-like activity. The discussion that follows will clarify several important diagnostic issues. An annotated bibliography is included for those interested in learning more about this topic.

Case Presentation

Ms. A, a 40-year-old, heavily tattooed woman with a history of bipolar disorder and alcohol dependence, was rushed to the hospital from jail after she wrapped a cord around her neck in a suicide attempt. During her evaluation in the Emergency Department (ED), she was awake, alert, irritable, and minimally cooperative. A computerized tomographic (CT) scan of the head revealed low-density abnormalities in the left frontal, parietal, and occipital lobes consistent with venous infarctions (secondary to the hypoxia sustained during her hanging). While in the ED, Ms. A had a number of seizure-like episodes (with clonic, jerking activity in her upper extremities). The medical team felt that these episodes were unlike tonic-clonic seizures seen in other patients; when they placed these symptoms in the context of Ms. A's angry and provocative manner, the team suspected pseudoseizures.

What Neuropsychiatric Manifestations Occur Commonly After Stroke?

Poststroke depression is a common psychiatric complication of stroke. Approximately 20% of patients who sustain a stroke meet criteria for major depressive disorder in the poststroke period; another 20% meet criteria for minor depression following stroke. Rapid diagnosis and treatment of poststroke depression are crucial, as rehabilitative efforts in the days following a stroke are critical in the overall functional recovery of poststroke patients. Left untreated, episodes of poststroke depression last for months and even years. Patients who have poststroke depression appear to have less ability to participate in their rehabilitation, and some studies^{1,2} suggest that poststroke depression leads to a worsened long-term functional outcome.

A number of psychosocial risk factors appear to increase the likelihood of developing poststroke depression. These include a history of major depression, poststroke social isolation, living alone, and, possibly, a family history of major depression. In addition, the risk of developing poststroke depression also appears to correlate with the severity of physi-

cal disability resulting from the stroke. Other variables, including cognitive impairment, age, and gender, have not been consistently associated with the development of poststroke depression.

Poststroke anxiety is also common; approximately one fourth of poststroke patients meet criteria (except for duration criteria) for generalized anxiety disorder (GAD) in the poststroke period. This poststroke anxiety is also associated with decreased functional recovery, which can persist for years after the stroke. Patients with GAD in the acute poststroke period appear to have decreased abilities to perform activities of daily living (ADLs) when compared to poststroke patients without anxiety. Poststroke mania occurs less frequently; it develops in less than 1% of poststroke patients. Symptoms of poststroke mania are similar to those of primary mania.

Another neuropsychiatric manifestation of stroke is a "catastrophic reaction," a collection of symptoms (involving intense desperation and frustration) that is uncharacteristic of the patient's prestroke personality. This occurs in roughly 10% of poststroke patients and is strongly associated with poststroke depression as well as a personal and family history of psychiatric disorders.

Finally, pseudobulbar affect, a clinical syndrome involving frequent and easily provoked spells of emotion (typically manifest by laughing and crying), is seen in approximately 10% to 15% of poststroke patients. In its most common form, brief fits of crying or laughing occur with appropriate changes in mood; in more serious cases, crying or laughing may develop in situations inappropriate to the context.

Is There a Correlation Between Lesion Location and the Development of Poststroke Neuropsychiatric Sequelae?

Possibly. Controversy exists with regard to the correlation between lesion location and poststroke depression. Initially it was thought that the frontal lobes and a right parietal location were most frequently associated with poststroke depression. However, more recent analyses (including a large meta-analysis by Carson and coworkers³) have found no correlation between lesion location and poststroke depression. If there is a correlation between stroke location and the presence of poststroke depression, it appears that strokes of the left frontal cortex and left basal ganglia are most often associated with the development of poststroke depression.

Anxiety associated with poststroke depression is most often seen with left-sided lesions, while patients with isolated anxiety may more often have right-hemispheric lesions. Poststroke mania appears to occur most often with right hemispheric lesions, especially when they occur in the right orbitofrontal region or the right thalamus. Catastrophic reactions are strongly associated with left frontal strokes.

How Are Poststroke Mania and Depression Treated?

Poststroke affective disorders are treated in roughly the same way as primary affective disorders. Selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), stimulants, and electroconvulsive therapy (ECT) have all been effective in the treatment of poststroke depression. SSRIs may be the first-line treatment of poststroke depression, given that they do not carry the risk of orthostatic hypotension and cardiac conduction abnormalities associated with TCAs. In one double-blind study by Robinson and associates,⁴ however, nortriptyline was found to be both well-tolerated and superior to fluoxetine in the treatment of poststroke depression; therefore, TCAs should also be strongly considered for treatment of poststroke depression.

Psychostimulants have also been efficacious for treatment of poststroke depression. Given the importance of adequate rehabilitative efforts in the immediate poststroke period, the ability of these agents to act more rapidly than traditional agents makes them very attractive in the treatment of poststroke depression. Stroke itself is not a contraindication to stimulant use. However, because one is essentially giving the patient a mild cardiac stress test with stimulants, conditions such as uncontrolled hypertension, recent ventricular arrhythmia, tachycardia, or recent myocardial infarction would be relative contraindications to the use of stimulants. In addition, stimulants should also be avoided in patients who have a history of an adverse reaction to stimulants, who are concomitantly taking monoamine oxidase inhibitors (MAOIs), or who are psychotic. Newer antidepressants with effects on norepinephrine (e.g., venlafaxine or mirtazapine) have not yet been studied in patients with poststroke depression. However, other agents that affect norepinephrine, such as nortriptyline and psychostimulants, have been effective in the treatment of poststroke depression without causing adverse effects as a result of noradrenergic stimulation.

Controlled studies of poststroke mania have yet to be completed, although case reports have suggested that lithium, valproic acid, carbamazepine, clonidine, and neuroleptics may each be effective in the treatment of poststroke mania.⁵ Given that there is some evidence that anticonvulsant mood stabilizers may be superior to lithium in the treatment of secondary mania, and given the propensity for seizures in the poststroke period, mood stabilizing anticonvulsants may be the agents of choice in this population. Adjunctive neuroleptics and/or benzodiazepines can also be used while the dose of the anticonvulsant is being titrated upward.

Does Ms. A's History of Bipolar Disorder Make It More Likely That She Will Develop Mania?

The answer is unclear. It appears that patients who develop poststroke mania are more likely to have premorbid depression, as well as higher rates of a family history of

affective illness. Therefore, it is quite likely that a history of bipolar disorder would increase the risk of poststroke mania; however, conclusive data are not yet available.

Given the Neuroanatomic Distribution of Ms. A's Stroke, What Neurologic Deficits Might Be Expected?

A left frontal lesion can disrupt usual frontal functions. Difficulties with executive function (manifested as difficulty with clock-drawing and other tasks involving planning, organizing, and sequencing), perseveration, disinhibition, and apathy are possible manifestations. Language areas, specifically Broca's area, may also be affected and result in a Broca's aphasia (with intact comprehension, but with impaired repetition and fluency, resulting in so-called telegraphic speech).

A left parietal lesion may affect reading, writing, and calculation. Gerstmann's syndrome, manifest by dyscalculia, finger agnosia, left-right disorientation, and dysgraphia, is a classic manifestation of left parietal lesions, although it is rarely seen in its full form. If the lesion is left temporoparietal, it may affect Wernicke's area (left superior posterior temporal lobe) and result in an aphasia, with impaired comprehension and repetition, and intact "fluency" that consists of phrases or sentences that are out of context or nonsensical.

A left occipital lesion may affect right-sided visual fields and may result in dyslexia without dysgraphia.

How Might One Make the Diagnosis of Pseudoseizures in Ms. A?

Pseudoseizures have the following characteristics that may differentiate them from true seizures:

- A gradual onset over several minutes, with a prolonged duration of seizures (> 5 minutes) without hypoxia or other vital sign abnormalities
- Variable features or pattern; most true seizures have a stereotyped pattern
- A lack of self-injury (e.g., no tongue biting, incontinence, or self-harm)
- Out-of-phase jerking and nonrhythmic clonic activity
- Clonic movements of the trunk or pelvic thrusting; most true tonic-clonic seizures have only upper and lower extremity clonic activity
- Bilateral motor activity with preserved consciousness
- Avoidance of noxious stimuli during the event
- No postictal confusion
- Bilateral motor activity and loss of consciousness—with a normal electroencephalogram (EEG) at the time of the "seizure"
- Ability to recall events that occurred during the episode

It should be kept in mind that many individuals with pseudoseizures also have true seizure disorders. Moreover, many seizures (e.g., complex partial seizures) often have unusual manifestations (e.g., perceptual disturbances and sudden panic) and may not result in abnormalities on a standard EEG, even during the event. Therefore, one should carefully assess the possibility of true seizures in this patient, especially given her recent stroke.

If further observation and treatment of Ms. A suggest that pseudoseizures are present, a number of steps can be taken to relieve her suffering and reduce the frequency of her episodes. The clinician should explore with Ms. A the relationship between her psychosocial distress and the onset of her seizure-like episodes. It could be that these episodes are her body's way of telling her that she is under inordinate amounts of stress. The clinician can share his or her impression that such symptoms are likely to resolve over time, especially if she is able to express her emotions and to reduce her stress and distress. Referral to psychiatry should also be considered, not only to help with the treatment of her symptoms, but also to assess and treat comorbid depression and anxiety, which occur frequently among those with pseudoseizures. Unfortunately, there are no specific pharmacologic treatments for pseudoseizures; however, antidepressants and anxiolytics can alleviate the manifestations of comorbid psychiatric illness.

Drug names: carbamazepine (Tegretol and others), clonidine (Catapres and others), fluoxetine (Prozac and others), lithium (Eskalith and others), mirtazapine (Remeron), nortriptyline (Pamelor and others), valproic acid (Depakene and others), venlafaxine (Effexor).

REFERENCES

1. Schubert DS, Taylor C, Lee S, et al. Physical consequences of depression in the stroke patient. *Gen Hosp Psychiatry* 1992;14:69-76
2. Parikh RM, Robinson RG, Lipsey JR, et al. The impact of poststroke depression on recovery in activities of daily living over a 2-year follow-up. *Arch Neurol* 1990;47:785-789
3. Carson AJ, MacHale S, Allen K, et al. Depression after stroke and lesion location: a systematic review. *Lancet* 2000;356:122-126
4. Robinson RG, Schultz SK, Castillo C, et al. Nortriptyline versus fluoxetine in the treatment of depression and in short-term recovery after stroke: a placebo-controlled, double-blind study. *Am J Psychiatry* 2000;157:351-359
5. Robinson RG, Starkstein SE. Neuropsychiatric aspects of cerebrovascular disorders. In: Yudofsky SC, Hales RE, eds. *The American Psychiatric Publishing Textbook of Neuropsychiatry and Clinical Neurosciences*. 3rd ed. Washington, DC: American Psychiatric Publishing; 1997:723-752

ANNOTATED BIBLIOGRAPHY

Review Articles

Boon PA, Williamson PD. The diagnosis of pseudoseizures. *Clin Neurol Neurosurg* 1993;95:1-8
 —A thoughtful review that outlines a diagnostic approach that can help to distinguish pseudoseizures from true ictal activity. As part of this approach, the authors discuss features of seizure activity that may suggest pseudoseizures. In addition, the authors describe the use of video-EEG monitoring, adjunctive laboratory data, and psychiatric evaluation as part of a thorough investigative process to determine whether apparent

- seizure activity is consistent with the diagnosis of pseudoseizures.
- Ramasubbu R, Kennedy SH. Factors complicating the diagnosis of depression in cerebrovascular disease, pt 1: phenomenological and nosological issues. *Can J Psychiatry* 1994;39:596-600
- Ramasubbu R, Kennedy SH. Factors complicating the diagnosis of depression in cerebrovascular disease, pt 2: neurological deficits and various assessment methods. *Can J Psychiatry* 1994;39:601-607
- An interesting 2-part series that outlines the difficulties associated with diagnosing depression in the poststroke period. The first article describes the difficulty with using standard diagnostic criteria for a depressive episode when a medical illness may be causing a number of neurovegetative symptoms. It also considers the significance of apathy, catastrophic reaction, and other symptoms in the diagnosis of poststroke depression. The second article discusses neurologic symptoms, such as aphasia and aprosodia, that can further confound the diagnosis of depression. This article ends with a discussion of various assessment tools that may be useful in the diagnosis of poststroke depression.
- Robinson RG. Neuropsychiatric consequences of stroke. *Annu Rev Med* 1997;48:217-229
- Robinson RG, Starkstein SE. Neuropsychiatric aspects of cerebrovascular disorders. In: Yudofsky SC, Hales RE, eds. *The American Psychiatric Publishing Textbook of Neuropsychiatry and Clinical Neurosciences*. 3rd ed. Washington, DC: American Psychiatric Publishing; 1997:723-752
- A clearly written and well-organized chapter that details the vast array of potential neuropsychiatric consequences of stroke. The chapter describes the epidemiology, presentation, and treatment of poststroke psychiatric disorders (depression, mania, psychosis, and anxiety). In addition, poststroke neuropsychiatric phenomena, such as pseudobulbar affect and aprosody, are reviewed.
- Bowman ES. Pseudoseizures. *Psychiatr Clin North Am* 1998;21:649-657
- A useful review of the diagnosis of pseudoseizures. The article includes a helpful discussion of the differential diagnosis of apparent seizure activity and lists a number of neurologic and psychiatric factors that can help to confirm (or to argue against) the presence of pseudoseizures. The author makes note of the frequent co-occurrence of epilepsy and pseudoseizures that can further complicate diagnosis.
- Carson AJ, MacHale S, Allen K, et al. Depression after stroke and lesion location: a systematic review. *Lancet* 2000;356:122-126
- A systematic review of 48 studies that investigated the association between the lesion location of a stroke and the subsequent onset of poststroke depression. The authors found no support for a correlation between lesion location and poststroke depression.
- Chemerinski E, Robinson RG. The neuropsychiatry of stroke. *Psychosomatics* 2000;41:5-14
- Two comprehensive reviews of poststroke psychiatric syndromes. Poststroke depression, mania, and anxiety are discussed, as are pseudobulbar affect and catastrophic reactions. Epidemiology, diagnosis, and management are outlined.
- Ouimet MA, Primeau F, Cole MG. Psychosocial risk factors in poststroke depression: a systematic review. *Can J Psychiatry* 2001;46:819-828
- A comprehensive review of the 25 studies examining the psychosocial risk factors for poststroke depression. The authors found that a history of depression, social isolation, living alone, language abnormalities, and functional impairment were the strongest psychosocial correlates of poststroke depression. In contrast, cognitive impairment did not appear to be associated with poststroke depression. For many other factors (such as family history of mood disorders, age, and sex), there were mixed results or a paucity of data.
- Whyte EM, Mulsant BH. Post stroke depression: epidemiology, pathophysiology, and biological treatment. *Biol Psychiatry* 2002;52:253-264
- An up-to-date, systematic, and well-written review of the epidemiology, etiology, and treatment of poststroke depression. The authors review the 14 most methodologically sound studies on poststroke depression and use the results from these studies to discuss important topics in poststroke depression. The authors use these data to comment on prevalence, episode length, etiopathology, biological and psychosocial risk factors, and treatment of poststroke depression. They conclude that poststroke depression is multifactorial in origin, involving numerous biological and psychosocial variables.

Original Articles

- Parikh RM, Lipsey JR, Robinson RG, et al. A two year longitudinal study of poststroke mood disorders: prognostic factors related to one and two year outcome. *Int J Psychiatry Med* 1988;18:45-56
- A prospective study of 103 stroke patients that examined the effects of multiple variables on poststroke depression at 1 and 2 years after index hospitalization. The authors found that left anterior infarction, in-hospital depression, and in-hospital physical impairment all predicted a greater likelihood of depression 1 year later. Furthermore, they found that in-hospital poststroke depression significantly correlated with future physical impairment.
- Parikh RM, Robinson RG, Lipsey JR, et al. The impact of poststroke depression on recovery of activities of daily living over a 2-year follow-up. *Arch Neurol* 1990;47:785-789
- This study prospectively followed 63 poststroke patients over a 2-year period; 25 had poststroke depression and 38 were nondepressed. Although ability to complete ADLs, cognitive impairment, and social functioning were comparable between the 2 groups during the initial hospitalization, significant differences appeared over the follow-up period. Patients with poststroke depression during the index hospitalization had significantly greater impairments of physical activities and language function when compared to patients who were nondepressed during their index hospitalization.
- Robinson RG, Schultz SK, Castillo C, et al. Nortriptyline versus fluoxetine in the treatment of depression and in short-term recovery after stroke: a placebo-controlled, double-blind study. *Am J Psychiatry* 2000;157:351-359
- A study of 104 depressed patients who received nortriptyline, fluoxetine, or placebo for a 12-week study period following stroke. The authors found that patients with poststroke depression treated with nortriptyline had a significantly higher response rate than did those in the other 2 groups. Furthermore, the patients who received nortriptyline had improvements in anxiety and in their ability to complete ADLs when compared to those in the other 2 treatment groups. All treatments were well-tolerated in this study.
- Wiart L, Petit H, Joseph A, et al. Fluoxetine in early poststroke depression: a double-blind placebo-controlled study. *Stroke* 2000;31:1829-1837
- A placebo-controlled, double-blind trial of fluoxetine for the treatment of poststroke depression. Thirty-one patients with poststroke depression were enrolled and treated with either fluoxetine or placebo. The group that received fluoxetine had significantly higher response rates (63%) than did the group that received placebo (31%) over the 45-day study period. There were no significant differences in functional, cognitive, or motor improvement between the groups. Fluoxetine was well-tolerated in this small study. These results confirmed prior findings that selective serotonin reuptake inhibitors (e.g., fluoxetine and citalopram) are effective in the treatment of poststroke depression.
- Carota A, Rossetti AO, Karapanayiotides T, et al. Catastrophic reaction in acute stroke: a reflex behavior in aphasic patients. *Neurology* 2001;57:1902-1905
- This study evaluated 326 first-time stroke patients for the presence of a catastrophic reaction. The authors found that 12 patients (4%) manifested a catastrophic reaction. All such patients had left-hemispheric strokes, and all had aphasia. The presence of catastrophic reaction was closely correlated to the presence of poststroke depression; 75% of the patients who had catastrophic reactions also had poststroke depression.