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Case 1-2019: A 34-Year-Old Veteran with Multiple Somatic Symptoms

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PRESENTATION OF CASE

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Dr. Timothy J. Petersen: A 34-year-old man was evaluated at this hospital because of headaches, cognitive changes, mood symptoms, flashbacks, chest pain, arm tingling, and gastrointestinal symptoms. The patient had served as a special operations combat medic in the U.S. Army Rangers for 8 years. He served in Operation Iraqi Freedom, completing three tours of duty.

The patient had had multiple traumatic injuries and experiences during training and deployment. Nine years before the current evaluation, during a parachute-jump training, he had a syncopal episode. Afterward, he could recall only that he had awoken on the ground while a colleague was packing his parachute. He had 3 weeks of headaches, stiffness of the cervical and thoracic spine, and difficulty sleeping.

Eight years before the current evaluation, the patient was hit by an explosive blast wave. Afterward, he reported “cloudy” mentation. While he served as the company medic, he was a first responder in two cases in which a soldier had committed suicide.

Three years later, during his third deployment, the patient was involved in a motor vehicle accident as a helmeted back-seat passenger. The armored fighting vehicle rolled approximately 9 m into a canal, and the patient was pinned under several men. He had blunt trauma to the head and reportedly lost consciousness for 20 minutes; he had a concussion and traumatic injuries of the head and face, including a hard-palate fracture. He subsequently had headaches and difficulty eating and breathing because of lip and nose swelling.

In the years after that accident, two types of headache persisted. The patient described the first type of headache as bitemporal pain, above the ears, that occurred a few times per week and was pounding in quality, triggered by certain noises or emotional conversations, and associated with nausea; he used rizatriptan for relief. He described the second type of headache as a “sharp, electrical” sensation, generally in the posterior occiput, that was constant and associated with neck

pain on turning of the head, sonophobia, photophobia, and nausea; he received botulinum toxin injections for temporary relief.

After the patient's third deployment ended, his wife noticed that he placed kitchen items in the wrong location, became lost while grocery shopping, and was unable to recall the birth of his first daughter. The patient expressed difficulty adjusting to a postdeployment routine, which included child care. He mentioned that he missed his level of entrusted responsibility in the Army Rangers platoon. He reported having "deep, lingering pain at deaths of friends and exposures to children in dire circumstances" and "thinking philosophically about death" but did not report suicidal or homicidal ideation. He rarely left the house except for appointments with doctors; he expressed difficulty making friends because he felt "frustration with trivial topics," and he was self-conscious about being forgetful. Mood swings, headaches, emotional distance, personality changes, irritability, fluctuating appetite with intermittent nausea, and insomnia and poor sleep were also reported. He avoided such places as shopping malls because they made him feel dizzy. He started to consume large quantities of whiskey daily.

Between 3 and 5 years before the current evaluation, while the patient was still in the military, he sought medical and psychiatric care on three occasions. During the first evaluation, duloxetine was prescribed, but it resulted in a rash and peeling of the skin. Three years before the current evaluation, he received inpatient treatment at a military hospital, which included psychotherapy sessions and muscle relaxation and breathing exercises. Two years before the current evaluation, various medications — including sumatriptan, ibuprofen, prednisone, topiramate, and amitriptyline — were tried, with varying degrees of success.

Twenty-two months before the current evaluation, the patient was honorably discharged from the military, and he moved to New England. Thirteen months before the current evaluation, his condition was assessed by a social worker, psychologist, physical therapist, and neurologist at another hospital. He reported being "constantly on guard" and "easily startled," as well as having anhedonia, detachment, difficulty concentrating, anorexia, and fatigue. He reported us-

ing sarcasm, defensiveness, and intellectualization as coping mechanisms. A review of systems was notable for a reduced ability to move the head and neck to the left and "clicking" with motion of the neck, both of which diminished modestly with physical therapy. Laboratory test results are shown in Table 1. The patient underwent a 3-month course of outpatient psychotherapy but then stopped because of a lack of connection with his provider.

Five months before the current evaluation, the patient reported having flashbacks with associated emesis. The next month, he reported that his previous concussion was "acting up." He described having a "hazy" feeling, verbal stuttering, and severe headaches, which he rated at 10 on a scale of 0 to 10 (with 10 indicating the most severe pain). The headaches lasted for days and were associated with sonophobia and photophobia; he used ice and ibuprofen for relief. He also began to have panic attacks in association with recall of memories. He described having a "rush of visions" of traumatic memories from childhood and the military and being "not able to turn them off"; lorazepam was prescribed. Recurrent pain and tingling of the left anterior chest and left anterior arm developed in association with these memories and later occurred independently of the memories. The patient treated himself for these symptoms with fans, cold baths, and benzodiazepines.

Two months before the current evaluation, multiple gastrointestinal symptoms developed. The patient had nonbloody, nonbilious emesis every morning, as well as persistent nausea, upper abdominal pain that was worse after eating, loose bowel movements alternating with constipation, difficulty initiating bowel movements, and eructation. He unintentionally lost 9 kg. He received prescriptions for tricyclic antidepressants, ondansetron, simethicone, and omeprazole for presumed irritable bowel syndrome. The next month, he had panic attacks of increased frequency and intensity and progressive symptoms, including atypical chest discomfort, heartburn, nausea, vomiting, and arm tingling. He sought attention in a local emergency department for panic attacks and fear that his heart was "feeling weak." Laboratory test results are shown in Table 1.

The patient was referred to this hospital; additional history was obtained from his wife. He had

Variable	Reference Range, Other Hospital	13 Mo before Current Evaluation, Other Hospital	1 Mo before Current Evaluation, Other Hospital
Hemoglobin (g/dl)	13.7–17.5	16.7	16.6
Hematocrit (%)	40.1–51.0	49.3	48.7
White-cell count (per mm ³)	4060–9400	7200	10,500
Platelet count (per mm ³)	124,000–335,000	307,000	338,000
Sodium (mmol/liter)	135–145	138	138
Potassium (mmol/liter)	3.5–5.0	4.5	3.9
Chloride (mmol/liter)	100–110	103	102
Carbon dioxide (mmol/liter)	20–30	26	26
Urea nitrogen (mg/dl)	7–25	12	11
Creatinine (mg/dl)	0.5–1.5	1.1	0.9
Glucose (mg/dl)	65–100	97	91
Aspartate aminotransferase (U/liter)	5–34	27	17
Alanine aminotransferase (U/liter)	7–52	62	21
Alkaline phosphatase (U/liter)	40–150	57	58
Thyrotropin (μ IU/ml)	0.35–5.00	1.84	0.91
Cholesterol (mg/dl)			
Total	<199	236	
High-density lipoprotein	>40	36	
Low-density lipoprotein	0–129	123	
Triglycerides (mg/dl)	<149	386	
25-Hydroxyvitamin D (ng/ml)	20–50	24.3	
Cortisol, morning (μ g/dl)	6–28	6.9	
Calcium (mg/dl)	8.5–10.5		10.4
Total protein (g/dl)	6.0–8.5		8.0
Albumin (g/dl)	3.5–5.0		4.9
γ -Glutamyltransferase (U/liter)	10–65		24
Total bilirubin (mg/dl)	0.2–1.2		1.2
Lipase (IU/liter)	8–70		27
Glycated hemoglobin (%)	4.0–5.7		5.4

* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586. To convert the values for triglycerides to millimoles per liter, multiply by 0.01129. To convert the values for calcium to millimoles per liter, multiply by 0.250. To convert the values for bilirubin to micromoles per liter, multiply by 17.1.

a history of obstructive sleep apnea, for which nightly continuous positive airway pressure had been prescribed, and he had undergone photorefractive keratectomy. A review of systems also revealed intrusive thoughts, hypervigilance, irritability, depressed mood, low energy, a feeling of burdening his family, and palpitations that were associated with anxiety and diffuse myalgia. He

had no dizziness, ataxia, vision changes, sensory dysfunction, hallucinations, repetitive behaviors, or focal weakness. He did not drive because of feelings of panic. He wore a hearing aid because of difficulty discriminating speech in the presence of background noise. He used a traction device for treatment of neck strain.

The patient's father had depression, and his

mother, father, and paternal uncle each had a history of alcohol and drug use disorders. The patient had been raised by his grandparents. A sister had died in her 20s from bone cancer. The patient lived with his wife and two healthy young children. He had not worked outside the home since his honorable discharge from the military, instead performing child care duties while his wife worked. He had completed 3 years of college; he had thought about additional schooling but felt discouraged because of forgetfulness. The patient had used chewing tobacco in the past but had not used any in 2 years. He consumed up to four caffeinated drinks daily and had only three or four alcoholic drinks monthly, which was a reduction from his past alcohol consumption. He smoked marijuana daily but used no illicit drugs. Medications included nortriptyline, omeprazole, pantoprazole, sucralfate, ondansetron, and as needed, simethicone.

On examination, the temperature was 37.1°C, the heart rate 94 beats per minute, the blood pressure 109/74 mm Hg, the respiratory rate 18 breaths per minute, and the oxygen saturation 97% while the patient was breathing ambient air. The weight was 86 kg, and the body-mass index (the weight in kilograms divided by the square of the height in meters) 26.4. The patient was well groomed, alert, cooperative, oriented, and lucid, with coherent speech. He was described as fidgeting, anxious, and irritable. The remainder of the cardiovascular, pulmonary, abdominal, and musculoskeletal examination was normal. A urine toxicology screen was positive for cannabinoids and negative for amphetamines, barbiturates, benzodiazepines, cocaine, opiates, and phencyclidine.

A diagnosis was made.

DIFFERENTIAL DIAGNOSIS

Dr. Abigail L. Donovan: This 34-year-old veteran served three tours of duty in Operation Iraqi Freedom, during which he had two traumatic head injuries and witnessed multiple traumatic events. Headaches, cognitive changes, mood symptoms, flashbacks, intrusive memories (with associated chest pain and arm tingling), and gastrointestinal symptoms developed.

This patient presented with physical and psychiatric symptoms, both of which must form the basis of my differential diagnosis. For any patient

with new-onset psychiatric symptoms, medical causes must be considered, particularly illnesses that are treatable or associated with severe outcomes — that is, illnesses that would have devastating consequences if they were missed.

NEUROLOGIC DISEASES

Cerebral aneurysm, vascular dissection, hemorrhage, ischemia, infections (meningitis and encephalitis), and pseudotumor cerebri can all cause headaches, mood symptoms, and cognitive changes. Tumors of the central nervous system (CNS) can cause these symptoms along with emesis and weight loss. Severe headaches or headaches in combination with certain “red flags,” such as focal neurologic signs or systemic illness, may indicate the presence of one of these serious underlying causes.¹

This patient described a history of headaches of more than 6 years, a finding that makes a diagnosis of neurologic disease highly unlikely. Over this 6-year period, an infection or cerebrovascular event would have led to focal neurologic signs, changes in vital signs, abnormal laboratory test results, or death. A CNS tumor associated with headaches and emesis would probably have caused ataxia or focal neurologic signs. Although imaging studies of the head would be obtained in this case to rule out a clinically significant abnormality of the brain or CNS, the chronic nature of this patient’s symptoms and the absence of other relevant findings most likely rule out a catastrophic neurologic diagnosis.

GASTROINTESTINAL DISEASES

Inflammatory bowel disease could explain the presence of gastrointestinal symptoms. However, although the onset of this disease can occur at any age, it typically occurs before 30 years of age, and the disease is usually associated with blood in the stool and not with vomiting or constipation, which were described by this patient.

Infections, including many that are commonly encountered in veterans who served in Operation Iraqi Freedom, can cause gastrointestinal symptoms, including diarrhea with fever, although they generally do not cause constipation. However, this patient’s exposures during active duty were not recent, and most infections cause time-limited diarrhea.

A vitamin B₁₂ or folate deficiency can cause

depression and can be related to malabsorption due to gastrointestinal disease. However, these deficiencies are typically associated with macrocytic anemia. Although a vitamin deficiency is unlikely in this case, it would be reasonable to obtain the vitamin B₁₂ and folate levels.

Irritable bowel syndrome could explain the patient's emesis, diarrhea, and constipation and is also often associated with depression, anxiety, and trauma. Irritable bowel syndrome seems to be a likely contributor to this patient's symptoms, but it does not explain several other features of this patient's presentation, including the headache, chest pain, and mental-status changes.

ENDOCRINE DISEASES

Hyperthyroidism could explain this patient's mood symptoms, anxiety, insomnia, diarrhea, and weight loss. However, he had a normal thyrotropin level, a finding that rules out this diagnosis.

TOXIC EXPOSURES

Veterans who served in Operation Iraqi Freedom have a number of potential toxic exposures, including depleted uranium, lead, sand and dust particles, burn pits, oil-well fires, and agents of chemical warfare.² However, these exposures are known to result in rashes, widespread pain, respiratory problems, or persistent fatigue, in addition to headaches and cognitive changes. The patient's symptoms and the timeline of illness are inconsistent with these exposures.

The urine toxicology screen revealed no evidence of opiate, amphetamine, cocaine, barbiturate, or benzodiazepine use. Opiate withdrawal can cause gastrointestinal symptoms, but these typically resolve within 1 week.

The patient's use of alcohol and cannabis could possibly explain his mood changes, anxiety (during withdrawal), cognitive changes, and headaches. Alcohol use disorder is associated with memory changes in the Wernicke–Korsakoff syndrome. However, this patient's memory changes predated heavy alcohol use. In addition, he had no ataxia, ophthalmoplegia, or confabulation. His current level of alcohol consumption would not explain his present symptoms. Cannabis use would not explain the severity of symptoms, particularly cognitive impairment. Although substance use may be a contributing factor, a substance use disorder is unlikely to be the primary diagnosis in this case.

MOOD AND ANXIETY DISORDERS

Bipolar disorder, major depressive disorder, and persistent depressive disorder could each explain the presence of mood changes and insomnia. A family history of depression and ongoing anxiety increase the likelihood of a mood disorder.

In bipolar disorder, episodic euphoria or irritability is accompanied by increased energy, activity, or speech, as well as grandiosity, distractibility, flight of ideas, or impulsivity. This patient had only irritability and insomnia, and those symptoms were chronic rather than episodic.

In major depressive disorder, episodic depressed mood is associated with anhedonia, anorexia, decreased energy, psychomotor changes, guilt, impaired concentration, or suicidality. Although several of these symptoms were present in this patient, they were chronic. Furthermore, the cognitive impairments appeared to be more severe than would be expected in depression.

Persistent depressive disorder is characterized by the presence of depressed mood and multiple neurovegetative symptoms for at least 2 years. This patient had chronic symptoms, but the severity of his cognitive decline was not entirely consistent with a persistent depressive disorder.

A panic disorder could explain the chest pain and tingling. In addition, anxiety disorders are highly associated with mood disorders.

TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI) has developed in 19% of veterans who served in Operation Iraqi Freedom or Operation Enduring Freedom³ and is the signature wound of these wars. Cognitive consequences of TBI (known as neurocognitive disorder due to TBI) include decreased attention, executive function, learning, memory, language, and social cognition.⁴ Physical manifestations include headaches, nausea, vomiting, diarrhea, constipation, and pain.⁵ Psychiatric consequences include personality changes, irritability, depression, anxiety, and substance use.^{5,6} TBI may explain this patient's mood symptoms, insomnia, cognitive decline, headaches, and gastrointestinal symptoms (either directly or mediated through irritable bowel syndrome).

POST-TRAUMATIC STRESS DISORDER

Post-traumatic stress disorder (PTSD) is present in 13 to 17% of veterans who served in Operation Iraqi Freedom or Operation Enduring Freedom.⁷

PTSD occurs after exposure to a traumatic event and is characterized by re-experiencing of the event (often with physiologic reactions to trauma cues), avoidance of trauma-related thoughts and external reminders, negative alterations in cognition or mood, and hyperarousal.⁴ PTSD could explain this patient's mood symptoms, insomnia, flashbacks, hypervigilance, startle, and panic attacks (with associated chest pain and tingling). Furthermore, veterans with PTSD are 4 times as likely to have chronic headaches and 3.5 times as likely to have irritable bowel syndrome as veterans without PTSD.^{8,9} A diagnosis of PTSD is the most parsimonious explanation of this patient's panic attacks (a physiologic reaction to trauma cues), rather than an independent panic disorder.

This patient's symptoms could be fully explained with two diagnoses: TBI and PTSD. How probable is it for these diagnoses to occur together? Veterans with TBI are 4 times as likely to have PTSD as veterans without TBI, and 17 to 43% of veterans with TBI also have PTSD.^{5,6,10}

DR. ABIGAIL L. DONOVAN'S
DIAGNOSES

Post-traumatic stress disorder.

Traumatic brain injury with secondary neurocognitive disorder.

PSYCHIATRIC DIAGNOSIS

Dr. Petersen: In 2013, the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5),⁴ included PTSD as a separate category in trauma- and stressor-related disorders, whereas the manual had previously included PTSD as an anxiety disorder. According to the current definition, this patient meets diagnostic criteria for a primary diagnosis of PTSD (Table 2).

A patient must meet eight DSM-5 criteria for the diagnosis of PTSD to be established. The first criterion is direct exposure or indirect exposure (e.g., involving a family member) to a traumatic event, such as the death of another person or threatened death, a serious injury, or sexual violence. In relation to the traumatic event, the patient must have symptoms in the following four clusters: intrusion (with at least one symptom present), persistent avoidance of stimuli associated with the traumatic event (at least one symptom), negative alterations in cognition and

mood (at least two symptoms), and marked alterations in arousal and reactivity (at least two symptoms). Symptoms in all four clusters must start after the trauma and persist for at least 1 month.

In patients with PTSD, the constellation of symptoms must lead to functional impairment or distress. This patient had difficulty connecting with his family, communicating, and performing activities that required organization skills, such as cooking and shopping. In addition, to establish the diagnosis of PTSD, substance use and other medical conditions must be ruled out. This patient's consumption of alcohol and marijuana was not likely to explain the extent of his functional impairment or its association with trauma.

DISCUSSION OF MANAGEMENT

Dr. Mireya F. Nadal-Vicens: Management of PTSD starts with a combination of psychotherapy and treatment with a selective serotonin-reuptake inhibitor or serotonin-norepinephrine reuptake inhibitor. In addition, mirtazapine, prazosin, tricyclic antidepressants, or phenelzine may be administered.¹¹ At this patient's initial evaluation, mirtazapine therapy was started, given its soporific and appetite-stimulating effects, but treatment was complicated by the development of a facial rash. Escitalopram therapy was started and was associated with no allergic reactions or unacceptable side effects.

Dr. Petersen: A key component of the patient's treatment was completion of 12 weekly 90-minute sessions of prolonged exposure therapy, which is an evidence-based, trauma-focused method of psychotherapy whose effectiveness is based on mechanisms of habituation and learning. During prolonged exposure, patients are required to confront traumatic memories through repeated imaginal exposures and to decrease avoidance by engaging in feared activities in a hierarchical manner (in vivo exposures). In addition to receiving these interventions, patients who undergo prolonged exposure therapy receive extensive psychoeducation regarding the nature of the effects of trauma and the mechanisms through which prolonged exposure exerts positive effects. Patients are given realistic expectations regarding the degree of difficulty of the treatment.

At the initiation of prolonged exposure, the

Table 2. Diagnostic Criteria for Post-Traumatic Stress Disorder.*

Criterion	Description	Characteristics of This Patient
Trigger	Patient has had direct or indirect exposure to a traumatic event, e.g., death of another person or threatened death, serious injury, or sexual violence.	He was a combat medic who, in the course of work, was exposed to major trauma and responded to suicides.
Symptoms that begin after trauma		
Intrusion	Patient has ≥ 1 of the following: involuntary recurrent memories, flashbacks, nightmares, or physical or emotional reactions to traumatic reminders.	He had intrusive thoughts and flashbacks, including scenes of death, and nightmares.
Avoidance of stimuli associated with the traumatic event	Patient has ≥ 1 of the following: avoids trauma-related thoughts and feelings or avoids cues and reminders.	He was guarded about previous experiences and avoided crowds and driving.
Negative alterations in cognition and mood	Patient has ≥ 2 of the following: amnesia in response to trauma, self-blame for trauma, inflexible negative beliefs, anhedonia, isolation, or difficulty expressing positive emotions.	He had thoughts of death and dying, self-blame for deaths of military friends, persistent negative emotional state, anhedonia, and detachment and isolation from his family.
Marked alterations in arousal and reactivity	Patient has ≥ 2 of the following: hypervigilance, startle behavior, aggressive or self-destructive behavior, difficulty concentrating, or sleep impairment.	He had irritability, hypervigilance, enhanced startle response, difficulty concentrating, and sleep disturbances.
Duration of symptoms	Patient has symptoms for >1 mo.	He had symptoms for 8 yr before the current evaluation.
Effect of symptoms	Patient has functional impairment or distress.	He had difficulty connecting with family, communicating, and performing tasks such as shopping and cooking.
Exclusions	Other underlying medical conditions and substance use have been ruled out.	His use of alcohol and marijuana was probably not a major contributing factor, and no other primary medical cause was identified.

* Criteria are adapted from the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5).⁴

patient and therapist collaboratively identify the index trauma, or the event that contributes most to PTSD symptoms. In this patient, the index trauma was an event in which he encountered two catastrophically injured Iraqi civilian girls who were close in age to his own daughters. During the imaginal exposures to this trauma, distress levels were closely monitored to track treatment-related progress and to identify the most troublesome aspects of the memory (“hot spots”). In parallel, the patient constructed a hierarchy of the most “life limiting” avoidant behaviors and systematically engaged in homework assignments to confront avoidance (i.e., shopping at the grocery store, attending his daughters’ school events, and taking public transportation). The key outcome that indicates treatment efficacy is a marked reduction in distress, both when recalling the index trauma and when engaging in previously avoided activities.

After the patient received acute psychotherapy and psychopharmacologic treatment with escitalopram and had consultations with several medical providers to assess somatic symptoms, his PTSD symptoms remitted. He still occasionally has subthreshold panic symptoms. His somatic symptoms have largely subsided, although he occasionally has headaches, which can be relieved with rest and ice. With regard to functional ability, his wife reports that he has fully reengaged in his role as a father and husband and no longer avoids activities of daily living (e.g., shopping at a grocery store). Of note, the patient reports that he enjoys home projects and pursues previous hobbies. He currently attends bimonthly maintenance follow-up appointments at this hospital.

Dr. David M. Dudzinski (Medicine): Dr. Kamenker-Orlov, would you comment on the prevalence of PTSD among returning soldiers and the response

of the Veterans Health Administration to this problem?

Dr. Yelena S. Kamenker-Orlov: Unfortunately, PTSD is highly prevalent among U.S. veterans. One study showed that among nearly 4.5 million patients who were treated at Veterans Affairs primary care clinics in 2010 to 2011, approximately 9% had a diagnosis of PTSD, more than 25% had depression, 8% had a substance use disorder, and 5% had anxiety.¹² However, among veterans who had returned from service in Iraq, the rate of PTSD was 16% — nearly twice the rate among all veterans.

This patient had somatic symptoms, which are very common manifestations of PTSD. Back pain is nearly twice as common among patients with positive PTSD screens as among those with negative PTSD screens (occurring in 40% vs. 22%), and so is joint pain (50% vs. 26%). Headaches are 3 times as common (32% vs. 10%). Gastrointestinal symptoms such as stomachache, nausea, and constipation are also common among patients with PTSD.

The time from the onset of symptoms to the initiation of treatment can be long. Only two thirds of veterans with PTSD report receiving specific treatment; less than half of those who

receive treatment report receiving any treatment in the previous year and less than one quarter report receiving specific mental health treatment. In response to these statistics, the Veterans Health Administration enacted a collaborative care model in which behavior health specialists were located in the same place as primary care practitioners and were immediately available for visits. The model was designed to improve the identification and treatment of veterans who have PTSD, as well as those who have depression, anxiety, and substance use disorders. Thereafter, mental health care was provided to nearly 6% of patients who were treated at Veterans Affairs primary care clinics, and the results of such treatment suggest decreased substance use, increased adherence to antidepressant regimens,¹³ enhanced patient engagement, and reduced stigma against accessing mental health services.¹⁴

FINAL DIAGNOSIS

Post-traumatic stress disorder.

This case was presented at Psychiatry Grand Rounds.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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