Case Report

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A Case of PTSD with Delayed Expression in a Patient with Advanced Alzheimer's Dementia

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ABSTRACT

Abbreviations: PTSD: Post-Traumatic Stress Disorder; MoCA: Montreal Cognitive Assessment; SBU: Senior Behavioral Unit; DSM: Diagnostic and Statistical Manual of Mental Disorders

Case Presentation

An 81-year-old white male with a medical history that includes Alzheimer's disease, hypercholesterolemia and a previous history of colon cancer and skin cancer presented to the emergency department from home due to escalating behavioral disturbances. At time of arrival, he was unresponsive to questions from nursing or providers. Instead, his eyes were shut, he ignored outside influences, and he was chanting and speaking loudly with minimal pauses. The patient is a combat veteran of the Vietnam War where he served three tours of duty; his third tour was in the Cambodian campaign. He appeared to essentially be relieving his time in Vietnam and is unable to be redirected to the present moment which is likely being mitigated by his ongoing advancing dementia. The patient appeared to be re-experiencing traumatic combat encounters. As if re-living specific combat encounters, he was heard asking, "where is my eye?" or "where is he?" He was also heard discussing artillery fire and shouting "help…help her…help!" He also appeared to be re-experiencing more possibly mundane moments of the war, stating "bring that chair here" while pointing to a corner in the room or "yes, Sergeant" in random instances. When asked his name, the patient initially responded "I know my name" in a chant-like manner. When asked a second time, he recited in full in the cadence that a soldier would if asked by a commanding officer. The patient sometimes nodded when asked if he was experiencing any auditory or visual hallucinations but was unable to elaborate and it was unclear if he understood the question. The patient continuously had his eyes closed during any interaction and despite sometimes opening them up initially when being talked to, he was unable to be reoriented.

When the patient's EKG tabs were being removed, he repeatedly asked, "what is changing" and had instances where his arms and hands moved in a repetitive manner, scrunching his blanket and passing it to whoever was talking to him on the side of his bed. It often appeared that while his body seemed to register external stimuli, his mind remained trapped in a state of re-experiencing. The patient was, otherwise, unable to answer any questions during our initial and all subsequent encounters. His family provided most details of the case. The patient was never previously diagnosed with post-traumatic stress disorder (PTSD), any trauma related disorder, or any other

mental health disorder. According to his family, he never complained of nightmares or re-experiencing symptoms. He was also described by his wife and son as kind and not prone to irritability or physical aggression. Though, his family admitted he may have experienced some avoidance symptoms, as he never discussed his experiences in the war. He also has no significant history of substance abuse. He was a previous alcohol user but was never a heavy drinker and stopped using altogether following his time in Vietnam.

His re-experiencing symptoms first manifested in 2021. The patient was first diagnosed with Alzheimer's disease by a neurologist over two years earlier in February 2019. This diagnosis was made clinically due to progressing memory decline and a baseline Montreal Cognitive Assessment (MoCA) score of 11 out of 30, indicating moderate cognitive decline. At this time, he was able to attend to most of his activities of daily living without assistance. He was having short- and long-term memory deficits, getting lost while driving, and having difficulty paying bills and managing finances.

He was prescribed donepezil 10 mg at bedtime, which he tolerated with no side effects. By April, his memory loss had worsened, he was no longer able to drive, and he was requiring more help with personal hygiene and other tasks. He also had new onset difficulties with sleep. His neurologist added memantine 5 mg twice a day to his medication regimen. His primary care provider also prescribed him trazodone 50 mg as needed for sleep. In July 2019, a second MoCA test was performed at his neurology outpatient visit to look for any improvement in the patient's memory and cognition in response to his current medication regimen, in which the patient scored a 12 out of 30. By 2020, the patient had started experiencing what his wife thought were mild auditory hallucinations. However, she did not believe these hallucinations were causing distress or that the patient had any personality changes. By 2021, he was dependent on his wife for all activities of daily living and he started having multiple day episodes of re-experiencing, which eventually remitted, where he engaged in non- stop chanting, singing, and talking loudly without ceasing. He also wandered in the house during these episodes and had impaired sleep. At this point, the patient's wife was still able to minimally communicate with him and redirect him during these episodes. His wife reported to the neurologist in 2023, that donepezil and memantine helped calm her husband and, she believed, prevented the escalation of his behavior. By mid-2024, he was no longer responding to any redirection and the re-experiencing behavior occurred almost nonstop. According to the patient's wife, she is able to calm him down by backing away and giving him space during these moments. He sleeps for short periods of time once he wears himself out. He has also had aggressive behavior at home during this time span, tearing up upholstery from a car and clenching his fist when his wife has tried to redirect him. He also became more fearful and resistant to riding in vehicles.

His oral intake had also declined, but his wife was able to feed him sweetened beverages. A few weeks prior to his emergency department presentation, his primary care provider discontinued his as needed trazodone and initiated valproic acid 125 mg twice a day and quetiapine 100 mg at night to attempt to regulate his behaviors and sleep. His wife was mixing these medications into sweetened beverages, primarily tea, to get the patient to take them. The patient's re-experiencing symptoms worsened in frequency and intensity while on these medications. The patient was seen by psychiatry in the emergency department. His quetiapine and valproic acid was discontinued. He was started on risperidone 0.5 mg given in liquid form twice a day and citalopram 10 mg in the morning. The patient was constantly chanting and screaming loudly while in the emergency department and was unable to be reoriented or calmed by his family. Several medications that could be given as needed for agitation, haloperidol and olanzapine, were also tried and failed, dosed as high as 10 mg every 4 hours as needed for agitation. He was eventually started on lorazepam which was helpful for mitigating the severity of the patient's episodes at least when given before his behavior had fully escalated. At intake, his vitals were largely stable, though his blood pressure was 91/49 and his heart rate was 63. His intake CBC, BMP, urinalysis, and urine drug screening were unremarkable, as were his subsequent lipid panel, folate level, and B-12 level. He did have some subclinical hypothyroidism. Due to his inability to feed himself, he had to be given medications and fed via a syringe where he would actively drink once the contents touched his tongue. He was admitted to the hospital's Senior Behavioral Unit (SBU) for stabilization and monitoring.

Clinical Diagnosis

The patient meets the diagnostic criteria for post-traumatic stress disorder with delayed expression. Most people who meet the criteria for PTSD do so within three months of the traumatic events. However, some patients do not do so for 6 months or much longer. For that reason, the Diagnostic and Statistical Manual of Mental Disorders (DSM) has included a delayed expression specifier since 1980. It is plausible the patient had some PTSD symptoms prior to onset of dementia. A recent systematic review concluded that some individuals may have an asymptomatic period; however, in most cases, those with delayed PTSD have symptoms during the first year after exposure to trauma [1]. Unfortunately, it is impossible to know this given the patient's advanced dementia. There are distinctive challenges in diagnosing PTSD in any patient with advanced dementia. These patients are often not capable of self-reporting symptoms or providing details of their personal history. Similarly, symptoms of PTSD can be mistaken for other psychiatric disorders or even attributed to dementia itself [2]. Given the severity of our patient's reexperiencing symptoms, many of the PTSD criteria were easily identifiable. The patient had experienced trauma first hand, he had negative cognitive changes in the form of a persistent negative emotional state where he was trapped in the trauma, significant sleep disruptions, and marked changes in arousal and reactivity due to his trauma. His intense intrusion and dissociative symptoms also directly led to his hospital admission. The most challenging portion of the DSM- 5 criteria to diagnose is whether the patient meets avoidance criteria.

Avoidance is difficult to assess in dementia patients. These patients are less mobile, live in fixed situations (e.g., nursing homes), and are not able to provide reliable insight into their own thought processes. A recent systematic review also found that the DSM-5 avoidance criteria was missing in most cases involving PTSD with delayed expression in those with dementia [3]. The patient likely meets this criteria given his unwillingness to communicate about the experiences he endured in war, prior to onset of dementia [4]. More interesting is family reports that the patient also has been resistant to any form of transport in vehicles, a marked recent change in behavior. Patient also has a diagnosis of major neurocognitive disorder due to Alzheimer's disease, with behavioral disturbances. The initial diagnosis of Alzheimer's disease was made by his outpatient neurology based primarily on a review of symptoms, including a slow and progressive decline in memory and ability to perform activities of daily living over an extended period of time. Lab work obtained upon admission also showed no obvious deficiencies that could present as dementia-like symptoms. His vitamin B-12 level, and folate level were within normal ranges. His thyroid panel showed only some subclinical hypothyroidism (Tables 1 & 2). His diagnostic imaging including CT and MRI scans without contrast showed microvascular ischemia but were unremarkable for any acute abnormalities.

Discussion

Recent research has demonstrated that combat exposure in veterans is a significant risk factor for cognitive decline and dementia [5]. Less well understood are the ways in which dementia may influence PTSD. There is an increased risk for PTSD with delayed expression in combat veterans with dementia. A 2020 systematic review of observational studies concluded as much and found that delayed-onset PTSD was most common in those with combat experiences that occurred before the age of 40 [6]. There are distinct correlations between the neurobiology of Alzheimer's dementia and PTSD. A large 2016 neuroimaging study found that individuals with PTSD have smaller amygdalas and hippocampuses [7]. Positron emission tomography and fMRI studies have shown that veterans with PTSD have reduced activity in the medial prefrontal cortex and increased activity in the amygdala [8]. It has been, similarly, found that in Alzheimer's disease there is hippocampal and amygdala atrophy, which contributes to hallmark symptoms such as disinhibition and cognitive decline [9].

It is plausible that structural atrophic changes in the brain, of those who have endured combat trauma but who have never been diagnosed with PTSD, are not only indicative of dementia but also of risk for delayed onset PTSD [10]. Similarly, dysregulation of neuroendocrine systems in Alzheimer's disease may also increase risk for later development of PTSD. One study found that Alzheimer's disease model mice reacted more strongly to trauma than other mice. This study found increased beta-amyloid levels associated with Alzheimer's dementia led to increased amyloid plaque deposition which activated corticotropin-releasing factor neurons and HPA axis responses, suggesting that Alzheimer's disease may actually contribute to higher rates of PTSD [11].

There are no distinctive pharmacological treatment strategies for PTSD with delayed expression that differ from standard approaches to this disorder. There is emerging research on treating PTSD in combat veterans with dementia, however most published work has focused on those with mild to moderate decline and highlights non-pharmacological strategies [12]. The most evidenced-based medications for PTSD are SSRIs and SNRIs, which target a deficiency of serotonin transport in the amygdala, and can help with re-experiencing symptoms and hyperarousal, as well as secondary symptoms of depression and anxiety. Stimulation of alpha receptors in the brain, which often occurs in PTSD, in the locus coeruleus, cerebral cortex, and limbic region is thought to disrupt higher order thinking, stimulate a fear response, and contribute to nightmares. Prazosin, an alpha-adrenergic blocker, reduces that stress response and is especially useful. Atypical antipsychotics also have evidence supporting their use to treat refractory symptoms and comorbid psychiatric issues [13]. Nonpharmacological strategies for PTSD are decisively more challenging in cases of advanced dementia. Though, there is some limited evidence that on-the-spot EMDR has produced positive results in patients with PTSD and advanced dementia [14]. Unfortunately, this resource was unavailable to our patient and, likely, would not have been feasible given his constantly closed eyes and his unceasing re-experiencing symptoms.

There have been case reports suggesting that donepezil, a cholinesterase inhibitor which is commonly prescribed to slow down the progression of dementia by helping reduce the degradation of the acetylcholinesterase enzyme in the brain, may worsen the symptoms of PTSD in combat veterans. Two case reports linked an increase of donepezil from 5 mg to 10 mg with the onset of delayed PTSD symptoms [15]. Another case report linked an exacerbation of PTSD to a trial of donepezil 5 mg [16]. In all of these cases, symptoms remitted after discontinuing the medication. Our patient started taking donepezil 10 mg in 2018 with no reported negative effect from his family. This medication was stopped upon admission to hospital, primarily due to concerns it could be contributing to his bradycardia and also due to the patient's difficulty taking medications. Stopping this medication did not seem to improve his symptoms in any significant way. It is worth mentioning that rivastigmine, another cholinesterase inhibitor, has shown promise as a potential augmentation for treatment-refractory PTSD since 2013 when it was used by mistake on a veteran from the Iran-Iraq war, who subsequently showed symptom improvement. There have been two other case reports, a non-controlled open trial, and a RCT supporting its benefits for chronic PTSD. A recent systematic review found the quality of the studies poor to moderate with significant limitations related to data collecting, reporting of results, and biased samples. For our purposes, the majority of the reported participants also were middle-aged and did not have a diagnosis of dementia [17]. Still, this evidence may be persuasive

enough for a provider to consider rivastigmine over donepezil for a patient with PTSD who would benefit from a cholinesterase inhibitor due to a co-occurring diagnosis of Alzheimer's disease.

Unfortunately, our patient proved resistant to many conventional pharmacological strategies. He was started on citalopram, which he was administered crushed in protein shakes and sweetened tea through a syringe. Fluoxetine was also considered due to it having an oral formulation but citalopram was chosen due to it having superior evidence for patients with dementia [18]. This was the patient's first trial of an SSRI and he was not on the medication for a sufficient period of time to determine its efficacy. Prazosin was considered but, ultimately, rejected due to the patient's inability to take the medication whole and there being insufficient evidence supporting the medication's continued efficacy if removed from the capsules. Clonidine was, similarly, considered due to ease of administration in patch form and evidence showing efficacy with PTSD related nightmares but rejected due to the patient having borderline hypotension. The patient did see improvement in symptoms with a combination of Risperdal titrated to 1 mg twice a day and lorazepam in 1-2 mg doses given for agitation. He was also taking memantine 10 mg twice a day for, at least, three years, but this medication, which does have some promise for PTSD, provided minimal relief. The patient received lorazepam often due to intense loud verbalization and behavioral issues that occurred with his re-experiencing symptoms. The patient had minimal response to haloperidol or olanzapine titrated to 10 mg each which were initially tried.

There is compelling evidence that benzodiazepines can worsen the effects of PTSD, as therapeutic effects decrease as tolerance to these medications grow whereas there can also be long-term cognitive effects related to attention, learning, and memory. Research also suggests that anxiety in PTSD likely involves the amygdala and hippocampus unlike other anxiety disorders [19]. Lorazepam was chosen due to an exhaustion of other options. After multiple days with little reported sleep due to constant re-experiencing symptoms, the lorazepam provided some, at least short term, reprieve for the patient. Risperdal was used primarily because it can be given in the oral concentrate form due to difficulties giving patient medications by mouth and also because of evidence supporting its use in dementia with behavioral disturbances. By the end of his stay at the SBU, the patient was more somnolent and was no longer chanting or talking loudly indicating this regimen potentially improved his symptoms. Palliative care was consulted early in the clinical process given the patient's advanced dementia. He was discharged to his home with hospice care services [20].

Labs Upon Admission

(Tables 1-4).

Table 1: Lipid and Thyroid Panel.

Lipids & CV Risk	09/29/24	
Cholesterol Total	249 mg/dL	
HDL Cholesterol	55 mg/dL	
Triglycerides	58 mg/dL	
LDL Calculated	82 mg/dL *	
Cholesterol/HDL Ratio	3	
Thyroid	**09/21/24**	**09/29/24**
TSH		4.760 mc Intl Units/mL* (H)
T3 Free	3.0 pg/mL*	
T4 Free	1.25 ng/dL	

Table 2: Vitamin B12 and Folate Serums.

Vitamins	09/19/24
Vitamin B12 Lvl	369 pg/mL
Folate Lvl	7.8 ng/mL

Table 3: Patient's Initial CBC.

CBC & Differential	9/24/24
WBC	9.9 10x3/uL
RBC	4.77 10x6/uL
Hgb	14.4 g/dL
Hct	42.3 %
MCV	89 fL
MHC	30 pg
MCHC	34 g/dL
RDW	13.2 %
Platelets	211 10x3/uL
MPV	6.0 fL
Neutrophil % Auto	77.8 %
Lymphocyte % Auto	9.4 % (L)
Monocyte % Auto	10.8 %
Eosinophil % Auto	1.4 %
Basophil % Auto	0.6 %
Absolute Neuts	7.7 10x3/uL
Absolute Lymphs	0.9 10x3/uL (L)
Absolute Monos	1.1 10x3/uL
Absolute Eos	0.1 10x3/uL
Absolute Basos	0.1 10x3/uL

Table 4: Patient's Initial CMP.

Routine Chemistry	09/21/24
Sodium Lvl	143 mmol/L
Potassium Lvl	3.7 mmol/L*
Chloride Lvl	112 mmol/L(H)
CO2	18 mmol/L (L)
Glucose Lvl	80 mg/dL
BUN	12 mg/dL
Creatinine Lvl	0.72 mg/dL
Calcium Lvl	8.3 mg/dL (L)

Physical Exam

Vitals & Measurements

T: 36.5 °C (Oral) HR: 57(Peripheral) RR: 18 BP: 91/49 SpO2: 97%

HT: 165 cm WT: 64.9 kg IBW: 61.41 BMI: 23.8

Diagnostic Reports and Imaging

12/2018, Per Requested Hospital Records

MRI Head w/o Contrast: Cortical atrophy with white matter changes in periventricular regions and centrum semiovale bilaterally consistent with a small vessel ischemic demyelination. No acute intracranial process. Mild mucoperiosteal thickening in ethmoidal sinuses. A mucous retention cyst is seen in the right maxillary sinus. Mastoid air cells clear.

7/2019, Per Neurology Visit

- Moca Score: 12/30
- PHQ2 & PHQ9 scores: 0

7/2022, Per Neurology Visit

- PHQ2 & PHQ9: Performed and Reviewed the appropriate Depression screening.
- Feeling Down, Depressed, Hopeless: Not at all
- Little Interest - Pleasure in Activities: Not at all
- Initial Depression Screen Score: 0

9/19/2024

- EKG: Sinus Rhythm with First Degree A-V Block, Low Voltage QRS, Borderline EKG with no previous EKG's available.
- Chest XR Impression: No acute radiographic abnormality of the chest.

9/20/2024

- CT Head w/o Contrast Impression: No CT evidence of acute intracranial abnormality. Global cerebral atrophy with presumed chronic microvascular ischemic changes.
- Repeat EKG: Sinus Rhythm with First Degree A-V Block, Left Axis Deviation, Low Voltage QRS, Nonspecific T wave abnormality when compared with EKG of 9/19/24. No significant change since previous tracing.
- Swallowing Screen: Yale Calculations: 5, Yale Results: Fail

9/23/2024

- Repeat EKG: Sinus Rhythm with First Degree A-V Block, Cannot rule out anterior infarct, age undetermined, Cannot rule out inferior infarct age undetermined abnormal EKG when compared with EKG of 9/20. Poor quality and previous EKG prevents comparison.

QT/QTc

432/459 ms.

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