

Threatening to burn the house down

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Mr. X, age 61, is experiencing behavioral and psychological symptoms of dementia, but so far none of the standard treatment approaches have helped. What would you do next?



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CASE Agitated and aggressive

Mr. X, age 61, who has Alzheimer's disease, is brought to the emergency department (ED) by his family after he is found to be confused, becomes physically aggressive with family members, and threatens to burn the house down. His family reports that earlier that day, he was paranoid that somebody was trying to kill him and he tried to leave the house. Mr. X has been experiencing visual hallucinations and delusional thoughts that made him aggressive towards his son. After an initial laboratory workup in the ED, Mr. X's bloodwork comes back positive for mild leukocytosis, indicating the possibility of an infectious etiology. Mr. X is admitted to the hospital for further evaluation of his altered mental status.

HISTORY Decline over 2 years

This is Mr. X's third inpatient admission for agitation and psychosis. His current medications—twice daily divalproex sodium extended release (ER), 250 mg every morning and 500 mg at every bedtime, and prazosin, 2 mg/d at bedtime—have been only partially effective. His medical history includes osteoarthritis, back pain, and heterozygous factor V Leiden (not on anticoagulation). He quit smoking tobacco several years ago and has no history of substance use. He has no family history of dementia. Previous trials

of cholinesterase inhibitors, antipsychotics, and antidepressants resulted in only minimal improvement in his agitation and psychosis.

A chart review shows that 2 years before his current hospital admission, Mr. X had presented to his primary care physician with slurred speech, forgetfulness, missing words, and transient reading difficulties. His initial laboratory workup and MRI came back normal. He was placed on short-term disability due to work-related errors. He was referred to the hospital's Memory Clinic 2 years ago, where his Mini-Mental State Exam score was 20/30, indicating mild cognitive impairment. Stroke workup was negative. Due to significant language deficits, a differential diagnosis for Alzheimer's disease vs primary progressive aphasia vs frontotemporal dementia was made. He screened positive for amyloid PET scan, which confirmed the diagnosis of Alzheimer's disease.

Neuropsychological testing showed similarities with logopenic variant of primary progressive aphasia, which in many cases is present in Alzheimer's disease. Mr. X was

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Clinical Point

Nonpharmacologic interventions are the first-line treatment for patients with BPSD

prescribed anticholinesterase inhibitors, including donepezil, 10 mg/d, and rivastigmine patch, 9.5 mg/d; and memantine, 10 mg/d, which he could not tolerate because of adverse effects. During the next year, Mr. X deteriorated and presented to the ED a few times with significant psychotic symptoms and aggression. He had a poor response to various pharmacologic and nonpharmacologic interventions during this time.

EVALUATION Continued problematic behaviors

During his hospitalization, Mr. X continues to be agitated and paranoid and is placed in restraints. He is unable to respond to his name and cannot follow simple verbal commands. Results of his laboratory workup are within normal limits. His mild leukocytosis resolves with no active signs of infection. Psychiatry is consulted for management of his behavioral and psychological symptoms of dementia (BPSD).

Mr. X is started on olanzapine and lorazepam as needed for agitation, and his twice daily divalproex sodium ER is increased to 250 every morning and 750 mg at every bedtime. However, Mr. X remains agitated and requires restraints. Olanzapine is switched from an as-needed dose to scheduled doses of 10 mg every morning and 15 mg at every bedtime, to address his psychosis and agitation.

On Day 24 of hospitalization, Mr. X's ammonia levels are checked and are found to be 69 μ /dL, which is high (normal range: 15 to 45 μ /dL). Divalproex sodium ER is eventually tapered and discontinued. Mr. X is started on carbamazepine, which is titrated to 400 mg twice daily and results in some improvement in his behavior. He continues to receive carbamazepine and is started on dextromethorphan-quinidine, 10 mg/d, and increased to 10 mg twice daily; however, Mr. X continues to be verbally aggressive with staff, throws food, wanders around, and tries to leave the hospital unit, so he is placed in restraints and continues to require a sitter.

What treatment approach would you consider next?

- a) nonpharmacologic approaches such as behavioral therapy
- b) pharmacologic treatment with a different antipsychotic
- c) electroconvulsive therapy

The author's observations

Dementia typically affects older adults, but its onset can occur before age 60. It is a syndrome rather than a specific illness; the most common types are Alzheimer's disease, vascular dementia, dementia with Lewy bodies, and frontotemporal dementia. Diagnostic clarity and an evidence-based treatment plan are crucial for improving the quality of life for both the patient and their caregivers. The *Table (page 41)* outlines the differential diagnosis of cognitive deficits. New-onset cognitive deficits warrant neuroimaging, and other testing may also be needed.

Behavioral and psychological symptoms of dementia

Noncognitive symptoms occur in 98% of individuals with dementia at some point in their disease and are often the most distressing to both caregivers and patients.¹ Behavioral and psychological symptoms of dementia, including apathy, depression, sleep disorders, hallucinations, delusions, psychosis, agitation, and aggression, are exceedingly prevalent.² Although these symptoms pose a significant burden, there are no clear published treatment guidelines; however, the American Psychiatric Association and the American Geriatric Society recommend using nonpharmacologic approaches as the first-line of treatment for patients with BPSD.^{3,4}

Nonpharmacologic treatments

Due to the unfavorable adverse effects profiles of medications commonly used to treat dementia, nonpharmacologic treatment



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Table

Differential diagnosis of cognitive deficits

Disease/condition	Hallmark features
Alzheimer's disease	Cognitive decline, language deficits, apraxia, agnosia, and eventual functional decline
Frontotemporal dementia	Changes in personality and behaviors, involves temporal and frontal lobes, early language difficulties
Vascular dementia	History of cerebrovascular accidents, stepwise decline
Dementia with Lewy bodies	Visual hallucinations and rigidity (parkinsonism features), sensitivity to antipsychotics
Delirium	Acute onset, fluctuating sensorium, sundowning
Hypothyroidism	Cold intolerance, fatigue, constipation, weight gain, dry skin, myalgia
Normal pressure hydrocephalus	Urinary incontinence, gait changes
Medication-induced	Anticholinergics, barbiturates, other sedative-hypnotics
Depression	Sadness, hopelessness, anhedonia, guilt, suicidal ideations
Tumor	Headaches, neurologic deficits
Chronic alcohol use	History of alcohol use, nystagmus, broad-based gait (rule out Wernicke-Korsakoff syndrome)
Other potential causes of cognitive deficits	Vitamin B12 deficiency, niacin deficiency, Creutzfeldt-Jakob disease, neurosyphilis, HIV infection, systemic lupus erythematosus, multiple sclerosis, Huntington disease, traumatic brain injury
HIV: human immunodeficiency virus	

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Pharmacologic therapies for patients with BPSD should be used when nonpharmacologic approaches are unsuccessful

approaches have always played a crucial role for managing BPSD. Interventions such as music therapy, aromatherapy, art therapy, behavioral therapy, reality orientation, tailored activities, and physical exercises, have shown promising results for alleviating BPSD.⁵⁻⁷

Pharmacologic treatments

Pharmacologic therapies should be used when nonpharmacologic approaches are unsuccessful, or when a patient is at imminent risk to harm themselves or others.

Antipsychotics. Although there is conflicting data regarding the use of antipsychotics in older adults, these agents are the most common pharmacologic treatment for patients with BPSD. Several studies examining the efficacy of antipsychotics for treating BPSD have demonstrated an increased risk of cerebrovascular events, including stroke and death due to any cause.⁸ While the use of antipsychotics increases the risk

of mortality in older adults, the absolute risk is still low.⁹

Antipsychotics used to treat BPSD include:

- Risperidone is well studied in older adults and has shown benefit for treating aggression, agitation, and psychosis.¹⁰
 - Quetiapine has a favorable adverse effects profile and may help improve sleep and reduce anxiety.¹⁰
 - Olanzapine. Low-dose olanzapine has been modestly effective in decreasing agitation and aggression in patients with Alzheimer's and vascular dementias.¹¹
 - Aripiprazole has shown modest benefit in treating psychosis and agitation in patients with dementia but may be associated with insomnia or activation symptoms at lower doses.¹⁰
 - Ziprasidone. Case reports have found benefit with oral and injectable forms.¹²
- Antidepressants.** In the CitAD study, which was a placebo-controlled randomized trial,

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ECT may be an option for patients with BPSD who do not respond to multiple pharmacologic treatments

Related Resources

- Van den Berg JF, Kruithof HC, Kok RM, et al. Electroconvulsive therapy for agitation and aggression in dementia: a systematic review. *Am J Geriatr Psychiatry*. 2018;26(4):419-434.
- Kales HC, Mulsant BH, Sajatovic M. Prescribing antipsychotics in geriatric patients: Focus on dementia. *Current Psychiatry*. 2017;16(12):24-30.

Drug Brand Names

Aripiprazole • Abilify	Lorazepam • Ativan
Carbamazepine • Tegretol	Memantine • Namenda
Citalopram • Celexa	Olanzapine • Zyprexa
Dextromethorphan-quinidine • Nuedexta	Prazosin • Minipress
Divalproex sodium ER • Depakote	Quetiapine • Seroquel
Donepezil • Aricept	Risperidone • Risperdal
Gabapentin • Neurontin	Rivastigmine • Exelon
Haloperidol • Haldol	Sertraline • Zoloft
	Trazodone • Desyrel, Oleptro
	Ziprasidone • Geodon

citalopram titrated to a target of 30 mg/d was found to be effective in reducing BPSD.¹³ However, QTc prolongation limits the use of citalopram. Sertraline was studied in 1 small, randomized trial against haloperidol but showed no additional benefit.¹⁴

Mood stabilizers. In a small, randomized trial, carbamazepine was helpful for patients with BPSD who were resistant to treatment with antipsychotics, with efficacy demonstrated over 6 weeks.¹⁵ No other mood stabilizers have had significant positive results in treating BPSD.¹⁶

Anxiolytic medications. Some research suggests that the occasional use of lorazepam, as necessary, is acceptable for patients with extreme agitation or aggression when behavioral interventions or sleep aids are ineffective.¹⁷ Various case reports and case

series have suggested gabapentin may be effective for BPSD.¹⁸

Prazosin. In a small randomized placebo-controlled trial, the commonly used antihypertensive agent prazosin reduced agitation and aggression in patients with Alzheimer's dementia, at doses from 1 to 6 mg/d.¹⁹ Postural hypotension, the main adverse effect associated with prazosin, can limit its use.

Trazodone. Some research suggests trazodone can reduce irritability and aggression in patients with Alzheimer's disease.²⁰

Dextromethorphan/quinidine. In a 10-week phase 2 randomized clinical trial of patients with probable Alzheimer's disease dementia, combination dextromethorphan/quinidine reduced agitation and was generally well tolerated.²¹

For patients such as Mr. X who do not respond to multiple pharmacologic treatments, electroconvulsive therapy (ECT) may be an option.

TREATMENT A trial of ECT

Because Mr. X does not respond to the standard treatment protocols, the treatment team and Mr. X's family discuss the use of ECT to control his agitation. Consent is obtained from his legal guardian and Mr. X is medically cleared to receive ECT. Mr. X receives 3 ECT treatments per week. During the first week, Mr. X experiences post-treatment agitation and confusion. The frequency of ECT treatments is reduced to 2 treatments per week, and then 1 session per week. Mr. X starts to

Bottom Line

Behavioral and psychological symptoms of dementia are associated with poor outcomes and a greater burden of care. Nonpharmacologic interventions should be the first-line treatment. The risk of prescribing medications for older adults should be carefully weighed against possible benefits, and pharmacotherapy should be combined with nonpharmacologic options for optimum results. Electroconvulsive therapy can be considered when standard treatment options are not successful.

show improvement in his agitation and ECT is continued at 1 session per week for 7 weeks.

The authors' observations

Electroconvulsive therapy has been an effective treatment for patients with treatment-resistant depression and has shown benefit in treating other psychiatric conditions such as acute mania, catatonia, psychotic disorders, and Parkinson's disease.²² Its use as an off-label treatment for chronic neuropathic pain has also been well documented.²³ Although ECT is not indicated for treating agitation and aggression in patients with dementia, its effectiveness for these symptoms has been discussed extensively in the literature.^{22,24-26}

Electroconvulsive therapy treatment can be divided into 2 phases: an acute phase during which ECT is administered 2 to 3 times a week for 4 to 5 weeks, and a maintenance phase of weekly treatments for 4 weeks and then biweekly treatments for 8 weeks.²⁶ Although extensive research supports the safe use of ECT in older adults, concerns for worsening cognitive impairment can deter patients and families from agreeing to this treatment.

Adverse effects of ECT such as headaches and postictal confusion are generally mild and transient. Severe adverse effects such as seizures, severe confusion, and delirium are uncommon.²⁵ The number of ECT treatments required for a good effect ranges from 2 to 18, and the most common position for electrodes placement is bilateral. Outcomes can be measured by using rating scales such as the Cohen-Mansfield Agitation Inventory, Neuropsychiatric Inventory, Social Dysfunction and Aggression Scale, Clinical Global Impression scale, and Pittsford Agitation Scale.²⁵ Obtaining consent from patients with dementia is generally not possible because these patients generally lack the capacity to make medical decisions. Clinicians should refer to their state laws regarding medical-decision making in such cases. The patient's next of kin or medical

power of attorney should be contacted, and the risks and benefits should be discussed before starting ECT.

OUTCOME Lasting improvement

Due to Mr. X's improvement after ECT, on hospital Day 124, the restraints are removed and he no longer requires a sitter. He starts responding to his name and following simple verbal commands. Electroconvulsive therapy is tapered to every other week, and eventually stopped as his status improves. Mr. X continues to do well and is maintained on the same dosages of olanzapine, carbamazepine, and dextromethorphan-quinidine he had been receiving prior to discharge.

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ECT is not indicated for treating agitation and aggression in patients with dementia, but some evidence supports its use in such cases

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Although research supports the safe use of ECT in older adults, concerns for worsening cognitive impairment can deter its use

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