Donepezil-induced Visual Hallucinations in an Elderly Woman: A Case Report

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Introduction

- Dementia is a common illness, affecting 55 million people worldwide.[1]
- Cholinesterase inhibitors, such as donepezil, can delay the decline of cognitive function.[2]
- In America, in 2021, over 1 million patients were prescribed donepezil.[3]
- Cholinesterase inhibitors are not without risk and are on the Beer's list, due to risks of hypotension and bradycardia.[4] There are few documented cases of visual hallucinations caused by donepezil.[5]

Case Report

Initial Visit

- 87-year-old female evaluated at PCP with concerns of 1-year history of gradual memory loss with worsening nighttime mentation/agitation.
- Medical history was notable for uncontrolled insulin-dependent T2DM, HTN, CKD G3aA2, and gradual weight loss from ageusia/gastroparesis.
- Home medications include amlodipine 5 mg qD, atorvastatin 40 mg qHS, benazepril 40 mg qD, famotidine 20 mg qD PRN, Levemir 8u qD, metformin 1000 mg BID, metoprolol tartrate 37.5 mg BID, and multivitamins.
- Memory evaluation with MOCA was scored 13/30.
- Standard memory workup per AAFP guidelines was obtained (Table 1A,C,D). Brain imaging was also ordered.
- Shared-decision making was used to start Donepezil 5 mg and re-evaluate in 2 weeks.

Subsequent Complications

- Two days after starting donepezil, patient presented to the ED due to visual hallucinations where she saw her deceased husband's face superimposed on her current husband's body.
- Vitals were stable (Table 1A).
- Labs were notable for hyperglycemia with HAGMA, AKI, and hypomagnesemia, otherwise unremarkable. Urinalysis was not consistent with a urinary tract infection. Head CT without contrast (Figure 1) was negative for acute processes, but showed chronic small vessel changes.
- Patient was treated with insulin and IV fluids and discharged home without changes to home medications.
- Patient was evaluated by PCP 5 days after being evaluated in ED.

Results

A	Office	ED
BMI	19.3	19
RR	-	20 bpm
SBP	138 mmHg	111 mmHg
DBP	90 mmHg	85 mmHg
HR	88 bpm	87-101 bpm
T	97.7°F	97.9°F
O2	100% RA	100% RA

B	ED
Color	Yellow
Appear	Clear
Spec Grav	1.020
pH	5.0
Protein	30 mg/dL
Glucose	1000 mg/dL
ketones	15 mg/dL
Urobilinogen	Normal
Blood	Negative
Nitrite	Negative
Leukocyte Esterase	Negative
RBC	0-2
WBC	0-2
Bacteria	2+
Hyaline Cast	10-20
Squam Epithelial	0-5

C	Office	ED	Post-ED
Glucose	244 mg/dL	347 mg/dL	162 mg/dL
BUN	22 mg/dL	26 mg/dL	23 mg/dL
Creatinine	1.06 mg/dL	1.4 mg/dL	1.2 mg/dL
GFR	51	37	44
Sodium	138 mmol/L	135 mmol/L	136 mmol/L
Potassium	3.9 mmol/L	4.0 mmol/L	4.7 mmol/L
Chloride	103 mmol/L	94 mmol/L	101 mmol/L
CO2	22 mmol/L	19 mmol/L	25 mmol/L
AGAP	13	22	10 mmol/L
Calcium	9.2 mg/dL	10.0 mg/dL	10.4 mg/dL
Bilirubin Total	1.2 mg/dL	-	-
ALP	75 unit/L	-	-
SGPT/ALT	14 unit/L	-	-
SGOT/AST	15 unit/L	-	-
Total protein	6.2 gm/dL	-	-
Albumin	4.4 gm/dL	-	-
Globulin	1.8 gm/dL	-	-
Magnesium	-	1.3 mEq/L	-
TSH	1.19 mcunit/mL	-	-
Syphilis	NR	-	-
HgbA1c	8.6%	-	-
Folate	15.2 ng/mL	-	-
B12	1773 pg/mL	-	-

D	Office	ED
WBC	10.6 K/mcL	10.2 K/mcL
RBC	4.60 Million/n	4.60 Million/n
Hgb	12.6 gm/dL	13.8 gm/dL
Hct	39.0%	41.4%
MCV	94.7 fL	90.0 fL
MCH	30.6 pg	30.0 pg
MCHC	33.3gm/dL	33.3gm/dL
RDW	13.1%	12.6%
Platelets	239 K/mcL	272 K/mcL
NRBC	0.0%	0.0%
Abs NRBC	0.00 K/mcL	0.00 K/mcL
Neutro	73.4%	82.4%
Lymph	17.3%	11.5%
Mono	7.5%	5.4%
Eos	0.9%	0.1%
Basophil	0.6%	9.2%
IG	0.3%	0.4%
Abs PMN	7.78 K/mcL	8.41 K/mcL
Abs Lmyph	1.84 K/mcL	1.17 K/mcL
Abs Mono	0.80 K/mcL	0.55 K/mcL
Abs Eos	0.01 K/mcL	0.01 K/mcL
Abs Basos	0.06 K/mcL	0.02 K/mcL

Table 1. Comparison of outpatient and emergency department (ED) vital signs (A), metabolic panel (C), and complete blood count (D). Urinalysis in ED demonstrated in (B).

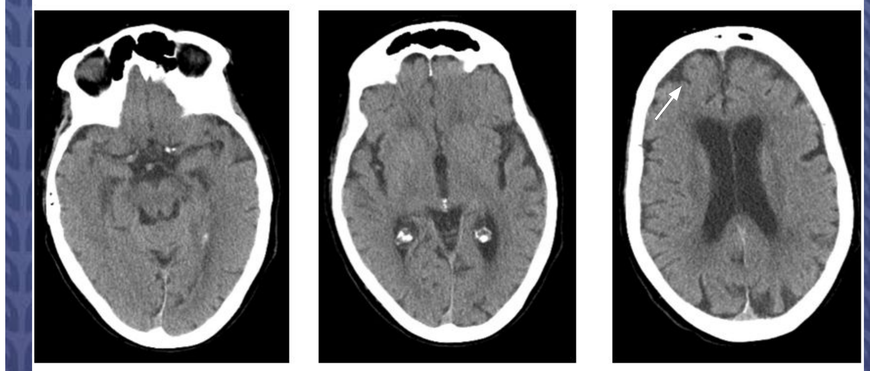

Figure 1. CT of head without contrast demonstrating chronic small vessel ischemic changes (white arrow) without other intracranial abnormalities.

Case Report (continued)

- She reported ongoing visual hallucinations: seeing a fan 'swinging sideways', a dog sitting in a chair, a pink rabbit going up the wall, and her deceased husband's face superimposed on her current husband's body.
- After reviewing ED workup, no clear organic etiology of the hallucinations was identified.
- Worsening of dementia with associated psychosis was entertained as a possible etiology. However, given the timing of symptom onset with initiation of donepezil, the decision was made to hold it.
- After holding donepezil, all hallucinations resolved within 72 hours and did not reoccur.

Discussion

- Pharmacovigilance databases reports 3% risk of hallucinations with acetylcholinesterase inhibitors.[6]
- There are few case reports documenting hallucinations secondary to donepezil, common side effects reported include GI, cardiovascular, dermatologic, and some CNS side-effects such as extrapyramidal symptoms.[5,6]
- It is hypothesized that when patients with preserved cholinergic function receive acetylcholine stimulation this can contribute to arousal and deficits in cognitive performance.
- Alternative etiologies for new hallucinations include Lewy-body dementia, progression of dementia, polypharmacy/medication side effect, delirium/sundowning, infection or metabolic encephalopathy.

Conclusions/Future Directions

- Our case highlights an underreported adverse effect of donepezil-induced hallucinations via a 'challenge-dechallenge' paradigm, emphasizing the importance of recognizing and managing such side effects in dementia patients on cholinesterase inhibitors.
- Consideration of more extensive testing to further clarify the specific etiology of underlying dementia (Alzheimer's dementia vs Lewy Body vs vascular)

References

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