Pseudodementia caused by severe depression

Edward Tobe

Department of Psychiatry,
Cooper Medical School of
Rowan University, University of
Medicine and Dentistry State of
New Jersey/School of
Osteopathic Medicine,
Camden, New Jersey, USA

Correspondence to

Dr Edward Tobe, edward.
tobe@comcast.net

SUMMARY

The diagnosis of pseudodementia may be difficult in a patient with a history of major depressive disorder. Clinical case history. A 70-year-old man with a history of major depressive disorder, in remission for 3 years, presented with confusion, agitation and cognitive disorder. The differential diagnosis included depression with pseudodementia, drug-induced dementia or Alzheimer disease. Mild cognitive improvement was noted after discontinuation of simvastatin. After 9 months of treatment for depression, the patient had remission that was sustained for >1 year, with mild residual difficulty remembering words of songs. The differential diagnosis of dementia includes major depressive disorder and adverse events from simvastatin.

BACKGROUND

Neurological consultation diagnosed this patient dementia of the Alzheimer type (DAT) with comorbid depression. He and his family faced emotional and fiscal calamity. The high prevalence of DAT in the patient's family history and the memories of caring for one of the demented maternal aunts made this dementia diagnosis a very real threat.

The overlapping signs and symptoms of dementia and depression can generate a medical debate. This case offers the rationale for each specialty and the rationale for treatment decisions. With an ageing population, these complex patients will require medical vigilance.

CASE PRESENTATION

A 70-year-old man presented with a 5-month history of confusion when reading simple material or watching television. He was unable to drive a car because he would become lost. He also had fatigue and fear of being alone, and he withdrew into his home because he was too confused to talk with people. He required his wife's continuous attention to direct him in everyday matters. He developed increasing agitation that was accelerated by lorazepam; when lorazepam was discontinued, the severe agitation lessened but continued as irritability.

Psychiatric history included a first episode of major depressive disorder at the age of 67 years, which went into remission within 3 months with psychopharmacological and cognitive therapy. The confusion at age 70 years occurred almost 3 years after remission from major depressive disorder and after 2 years without any psychotropic medicine. For 10 years before the diagnosis of major depressive disorder, he had been prescribed zolpidem and low-dose lorazepam for disrupted sleep, anxiety and somatic complaints.

The medical history included controlled hypertension, dyslipidaemia and obstructive sleep apnoea

that had been effectively treated with continuous positive airway pressure. He had a postdoctoral education and excellent vocational and avocational successes.

All blood studies including neuroendocrine studies were normal. MRI of the brain revealed minimal hippocampal atrophy, slightly more apparent on the left, with mild dilation of the temporal horns and coronal fissures, but no abnormal hippocampal signal. There was no evidence of multi-infarct dementia.

Neurological consultation showed depression, disturbed sleep-wake cycle, agitation and impairments in daily functional activities, memory, language, executive functioning and praxis. The neurologist elicited a history of subtle cognitive problems evolving during the previous 6 months. The neurologist opined that dementia was in the incipient stage and accelerated by the onset of the mood disorder. The patient was prescribed rivastigmine an anticholinesterase inhibitor, tapered from recently prescribed duloxetine because of possible noradrenergic adverse events (agitation), and started on mirtazapine.

Neuropsychological testing was performed (table 1). The neuropsychologist diagnosed severe depression without organic dementia, and opined that the findings suggested adequate memory for contextual information with mild decline in ability to learn, retain and encode discrete verbal memory. Visual memory and spatial skills were somewhat weak.

The neurologist disagreed with the interpretation of the neuropsychological studies because of inconsistencies in the data. The inability to comprehend conversations and follow driving instructions was deemed incompatible with a diagnosis of depression without hypokinesia. The patient did not manifest catatonia or major psychomotor retardation. Because there is no time limit, the Boston Naming Test is not affected by attention or concentration. On the Boston Naming Test the patient scored in the 14th percentile demonstrating anomia, a hallmark feature of the early language disturbance of Alzheimer disease.

Another medical question was the possible link of the onset of the patient's cognitive problems with the initiation of simvastatin. The internal medicine specialist felt that this association was highly improbable. Nevertheless, simvastatin was discontinued; within 1 week, the patient could understand the newspaper and television, but there were no other cognitive improvements. He remained ill with negative intrusive thinking, thoughts of death, fears of what people thought of him, problems communicating, fatigue and fears of insanity.

Due to the neurologist's criticism of the conclusions made by the neuropsychologist, another

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Table 1 Neuropsychological testing in a 70-year-old man with confusion, agitation, and history of depression

Test	Test component	Patient's standard score	Percentile ranking in population	Range
WAIS-IV	Verbal Comprehension Index	122	93	Superior
	Perceptual Reasoning Index	111	77	High average
	Working Memory Index	95	37	Average
	Processing Speed Index	86	18	Low average
WAIS-IV Verbal Subtests	Full Scale IQ (Prorated)	106	66	Average
	Similarities	13	—	—
	Vocabulary	15	—	—
	Arithmetic	7	—	—
WAIS-IV Performance Subtests	Digit span	11	—	—
	Block design	11	—	—
	Matrix reasoning	13	—	—
	Symbol search	7	—	—
Wechsler Memory Scale, Third Edition	Digit-symbol coding	8	—	—
	Raw Score: 16	7	16	—
	Mental Control			
	Wechsler Memory Scale, Fourth Edition			
Wechsler Memory Scale, Fourth Edition	Logical Memory I, raw score: 33	11	63	—
	Logical Memory II, raw score: 23	12	75	—
	Logical Memory Recognition, raw score: 20/30	—	>75	—
	Visual Reproduction I, raw score: 30	10	50	—
	Visual Reproduction II, raw score: 12	8	25	—
	Visual Reproduction Recognition, raw score: 4/7	—	26–50	—
Medical Symptom Validity Test		% Correct	—	—
	Immediate recognition	100	—	—
	Delayed recognition	80	—	—
	Total consistent	80	—	—
	Paired associates	60	—	—
	Delayed free recall	25	—	—
Boston Naming Test	Raw score: 51/60	—	14	Mild impairment
Controlled Oral Word Association	Total:33	—	14	Mild impairment
Semantic Fluency (animal naming)	Total:11	—	1	Moderate impairment
Trails A	52 s, no errors	—	10	Mild impairment
Trails B	77 s, no errors	—	42	Average
Geriatric Depression Scale	Score: 28	—	—	Severe
Beck Anxiety Inventory	Score: 9	—	—	Mild

WAIS-IV, Wechsler Adult Intelligence Scale, Fourth Edition.

neuropsychologist reviewed the neuropsychological data and agreed with the validity of the testing. Neuropsychological consultants emphasised: (1) that the patient had a prior episode of major depressive disorder, and the mood disorder was recurrent; (2) bradyphrenia due to depression might diminish some neuropsychological testing scores. The patient did better on the Trails B test than the Trails A test; Trails B test is more sensitive to frontal lobe pathology than Trails A test.

Hippocampal atrophy on the MRI could have occurred from either dementia or mood disorder.

Although aggressive treatment for depression could involve polypharmacy, somatic treatment and adverse events, we favoured a tentative diagnosis of severe major depressive disorder that required treatment until reaching remission. After 9 months of changing pharmacotherapy, the patient obtained remission that has been sustained for >1 year. Current daily medicines include duloxetine 60 mg, mirtazapine 30 mg, nortriptyline 25 mg and apripazole 1 mg. The need for an aggressive

polypharmacy was due to a treatment-resistant depression. The goal of treatment is remission. He became fully functional. There were only subtle residual complaints of struggling to recall well-known songs that he had sung to his children as babies.

DIFFERENTIAL DIAGNOSIS

Dementia, major depressive disorder and adverse events from simvastatin.

TREATMENT

Current daily medicines include duloxetine 60 mg, mirtazapine 30 mg, nortriptyline 25 mg and apripazole 1 mg.

OUTCOME AND FOLLOW-UP

Remission has been sustained for >1 year. He has subtle residual complaints of struggling to recall well-known songs that he had sung to his children as babies. The patient and his wife obtained a second opinion halfway through their treatment with

this office and 6 months after recovery at a tertiary care medical centre that offers a nationally recognised subspecialty in DAT. At 6 months after recovery, the subspecialty facility's evaluation determined that he did not have dementia. He was offered the centre's psychometric battery to evaluate potential cognitive decline. There were equivocal findings in reference to verbal list learning and cognitive flexibility. However, his functional rating scale score was normal. The centre offered their impression and recommendations:

Complex neuropsychiatric history with major depression and anxiety, likely past idiosyncratic statin-induced encephalopathy and borderline, nonspecific cognitive dysfunction. No noteworthy evidence suggesting neurodegenerative disease process.

At this time, the patient has been in remission for over 1 year. He requires ongoing multiple psychopharmacological agents.

DISCUSSION

Some patients with mood disorder present with severe impairments in verbal learning, synthetic cognition, memory, concentration, processing speed and praxis. Vegetative signs can be as extreme as catatonia. The study 'Melancholic Dementia' was published in approximately 1883 by Professor Albert Mairer, honorary doyen of the Faculty of Medicine of Montpellier.^{1 2} In the 19th century, physicians debated 'the interaction between dementia, depressive illness, general paralysis, and brain localization'.¹ There were differences in medical opinion about histopathological postmortem findings:

Mairer's observation that melancholic patients were found post-mortem to have changes in the temporal lobe led him to hypothesise that this area might be related to primary feelings of sadness and that the nihilistic delusions were in fact secondary developments made possible by the spread of the lesion to the cortex.¹

Advances in research methods have demonstrated that mood disorder is associated with pathologic metabolism and cellular morphology in specific brain tissues.³ Abnormal neuroplasticity can present as Alzheimer disease. Dementia that is confirmed on postmortem examination may have presented as a psychiatric disorder.⁴ We treated a patient that exemplified how we resolved the interdisciplinary debate about diagnosis, leading to changes in treatment and outcome.

The combination of the family's fear of dementia combined with inadequate medical specialty collaboration accelerated the stress for the patient and family. The neurologist was absolutely certain the patient suffered DAT and argued that the neuropsychological data were inconsistent. The neurologist diagnosed depression as secondary to DAT and did not perceive a need to prescribe various psychotropics that might adversely affect the patient. Perhaps physicians should consider avenues to enhance collaboration. A different opinion among colleagues creates a learning environment.

The patient had a pre-existing history of major depressive disorder. He remained in remission without medication for 2 years. The re-emergence of his illness was consistent with the high recurrence rate of major depressive disorder.^{5 6} There has

been controversy about whether the cholesterol-lowering statin drugs are related to cognitive disorder and/or mood disorder.⁷ For the above patient, subjective cognitive improvement occurred after the statin was discontinued. The decreased hippocampal volume on the MRI of the brain was misleading, because hippocampal changes may occur in depression, dementia and other diseases. Analysis of the diagnostic questions, assumption of the risk of polypharmacy in treatment-resistant depression enabled aggressive treatment that brought the patient into remission.

This case demonstrates that benzodiazepines pose risks especially in the elderly population. Although the patient took lorazepam and zolpidem for years, he experienced paradoxical disinhibition that improved immediately after discontinuing lorazepam. Benzodiazepine medicines can cause anterograde amnesia. Elderly population often have lower serum albumin levels creating greater vulnerability to CNS depression.

The lingering verbal memory complaint may have been caused by brain changes associated with depression.⁸

Learning points

- ▶ Dementia and mood disorder, especially severe mood disorder, have significant overlapping features even on MRI and neuropsychological testing.
- ▶ Clinical history must be thorough to weigh a differential diagnosis.
- ▶ Differences of opinion among physicians offer a learning opportunity that can benefit the patient as long as the patient is not put in the middle of the debate.
- ▶ Pharmaceutical agents have additional risks in the elderly population such as paradoxical disinhibition and memory loss.

Competing interests None.

Patient consent Obtained.

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