Dementia, Depression, or Both?
Differentiating in Older Patients

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Alfred's Case

A 75-year-old man is brought to your office by his wife. She tells you that there has been a gradual decline in his memory and problem-solving abilities over the last three years. About a year ago, he gave up driving and financial management. Three months ago, his appetite fell off. He also began sleeping poorly and complained of fatigue. Alfred repeatedly tells his wife that she would be better off without him. You find him restless and unhappy but alert. He scores 15/30 on a Mini-Mental State Examination. Other than signs of weight loss, the physical examination is unremarkable.

Rarely, depression can be confused with a dementia. The occurrence of late-life depression increases the risk of developing a dementia, and the two conditions frequently co-exist. The latter is the most likely explanation of Alfred's presentation. In this article I will briefly review the relationship between the two conditions.

Pseudodementia

This is an old term used to describe patients diagnosed with a dementia who turn out to have another psychiatric disorder, usually depression.[1] These patients are at risk of not being treated for a potentially reversible cause of their impaired cognition.

The concept of pseudodementia encourages physicians to perform a full diagnostic work-up in a patient presenting with a presumed dementia. While clinically significant depressive symptoms should be treated if found, this will very rarely fully reverse the cognitive impairment. Less than 1% of dementia cases are fully reversible.[2] A comprehensive assessment focusing on the features listed in Table 1 is usually able to distinguish between depression and dementia, but most of those with depressive symptoms and cognitive impairment have a dementia with associated psychological symptoms. There should be a search for depressive symptoms in an individual presenting with a suspected dementia; if discovered, these symptoms should be treated, but be careful not to raise excessive expectations on the part of patients and their families. Treatment of the depressive symptoms will likely not completely reverse the cognitive problems.

Risk of Dementia

Late-life depression increases the risk of developing a dementia by up to two fold, but it has been unclear as to whether depression is truly a risk factor for dementia or an early manifestation of a dementing illness. Recent studies suggest the latter.[3]

Table 1
Comparison of Select Features of Depression and Dementia

Indicator	Depression	Dementia
Mood	Develop a persistently sad mood over a period of weeks	Usually normal but can become transiently unhappy in reaction to events
Sense of Guilt or Worthlessness	Common	Rare
Suicidal Thinking	Common	Rare
Anxiety/Agitation	• Can develop over weeks • Often worse in the morning	• Seen as dementia progresses • Often worse in latter part of the day (sundowning) and in unfamiliar surroundings
Cognition	• Problems with concentration and focus that develop over weeks • Indecisiveness and anxiety about making mistakes	• Progressive, gradual decline in memory and other domains • Concentration normal early on
Concern about Cognitive Deficits	• Seem to exaggerate severity • Preoccupied with deficits	• Show little concern • Minimizes and often denies
Interest in Hobbies and Other Pleasurable Activities	Loss of interest in hobbies and formerly pleasurable activities over weeks	Gradual loss of interest and initiative over years
Physical Symptoms	• Changes in appetite over weeks — weight can be up or down • Over weeks can see either more or less sleep than usual • Frequent complaints of fatigue and, if depression is severe, can become "slowed down" (psychomotor retardation)	• Gradual loss of weight over years • Gradual disruption of normal sleep-wake cycles • Often less active but rare to see psychomotor retardation until dementia is advanced

Depressive Symptoms in Dementia

Depressive symptoms, which often fluctuate, are seen in up to 40% of patients with a dementia.[4] They cause distress, exacerbate the cognitive and functional impairments of the individual with dementia, reduce their quality of life, lead to caregiver stress and burden, and are potentially reversible with treatment.

The diagnosis of depression can be difficult in the setting of a dementia. Differentiating dementia-related apathy from the anhedonia (*i.e.*, loss of the capacity to experience pleasure) seen with depression is challenging. Apathy occurs in one-third to two-thirds of patients with Alzheimer's disease and is common in other forms of dementia as well. These patients seem indifferent, withdrawn, indolent, and indecisive. Apathetic patients require prompts and assistance to initiate an activity. In contrast with depressed patients, apathetic

ones typically don't have a sad mood, feel guilty, or express hopelessness (see Table 1).

A second challenge is diagnosing depression in more severely demented patients who are not able to give a reliable history. As self-report instruments like the Geriatric Depression Scale become problematic, you have to actively look for signs of depression like evident unhappiness, sadness, mood-congruent delusions (*i.e.*, any delusion with content consistent with a depressed state like the patient believing they committed a crime or are being persecuted), and recurring statements indicating guilt, hopelessness, helplessness, and worthlessness. Input from an informant is often required.[5] Behavioural disturbances like agitation, yelling, and refusing to eat can indicate an underlying depression, especially when they are accompanied by depressive symptoms. If in doubt, consider a trial of treatment.

Treating Depression in the Presence of Dementia

Studies of antidepressants in patients with dementia suffering from significant depressive symptoms have showed mixed results. The Health Technology Assessment Study of the Use of Antidepressants for Depression in Dementia (HTA-SADD) casts doubt on their utility. Compared to placebo, both sertraline and mirtazapine at therapeutic doses did not lead to significantly better outcomes while being associated with more adverse events.[6] It is important to note that the results of this study are not generalizable to those suffering from very severe depression, and it is possible that other antidepressants would work better. A stepped approach to management is currently recommended. As depression in dementia often resolves on its own, you initially monitor these patients (*i.e.*, watchful waiting) for up to three months if their symptoms are not too distressing. The second step would be low-intensely psychosocial interventions, such as planned participation in pleasurable activities, an exercise program, and problem-solving training for the caregivers of these individuals. The final steps entail moving on to more complex psychosocial interventions, medications, and/or rarely electroconvulsive therapy.[7]

Conclusion

While it is important to look for depressive symptoms in an individual presenting with cognitive impairment, remember that you are more likely to see the two conditions coexisting than see one masquerading for the other. Once detected, consider non-pharmacological interventions first and reserve antidepressants for those suffering from severe and/or refractory depressive symptoms. Dx

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