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PSYCHOGERIATRIC NOTE

Different pharmacological responses in late-life depression with subsequent dementia: a case supporting the reserve threshold theory

Key words: acetylcholinesterase inhibitors, cognitive impairment, dementia, late-life depression reserve threshold theory.

INTRODUCTION

Previous studies have demonstrated that patients with late-onset depression have several unique characteristics, including no previous depressive episodes, no family history of depressive disorders, comorbidity with cognitive impairment, presence of neuroimaging findings (especially white matter lesions identified as white matter hyperintensities on T2-weighted or fluid-attenuated inversion recovery magnetic resonance imaging), and refractoriness to antidepressant treatment. Lateonset depression is a well-known factor associated with the development of dementia. However, it is not clear whether late-onset depression is a risk factor or a very early symptom of dementia.

CASE REPORT

We experienced an interesting case involving a patient with late-life depression. The patient's two depressive episodes had different symptomatic profiles and responded differently to pharmacotherapy. This suggests that depression should be considered a risk factor for, not a prodromal syndrome of, dementia. A 78-year-old woman had been referred to our department because of her depressive and irritable mood. This was her first depressive episode, and there was no family history of psychiatric disorders. She clearly stated that she had experienced no recent negative life events and did not perceive her life situation as distressing. She was divorced and lived alone. She had a history of hypertension and ischaemic heart disease and took some medications for these disorders. Her depression level was not very severe, but she had moderate anxiety and irritability. She showed six of the nine Diagnostic and Statistical Manual of Mental Disorders, 4th edition, criterion symptoms

of a major depressive episode; thus, she was diagnosed with major depressive disorder and started to take sertraline (25 mg/day). The patient seemed to have minimal cognitive impairment concomitant with the depression, but she had occasionally mistaken her appointment time at the outpatient clinic. Ultimately, this symptom did not impair her daily life. Her depression fully remitted without an escalation of the antidepressant dose. She was discharged from the outpatient clinic just 1 year after her initial visit, as her remission status had remained stable for 6 months without any psychotropic medication.

Approximately 10 months later, she revisited our department with her daughter because her depression had recurred in the absence of any stressful life events. Her daughter said that the patient could not live alone because of her suicidal ideation, and she had lived with her daughter's family for several weeks preceding the visit. The patient now showed the full nine Diagnostic and Statistical Manual of Mental Disorders, 4th edition, criterion symptoms for a major depressive episode. Her depression was now considered quite severe, and she was admitted. Before admission, her depression had been treated again with sertraline, and the dose had been increased to 100 mg/ day for 6 weeks. However, the patient's depression had not improved at all. During her admission, some additional neuropsychological and neuroradiological examinations were administered, as dementia was suspected because of her clinically evident cognitive impairment. Her test results were as follows:

- Mini-Mental State Examination, 22
- Alzheimer's Disease Assessment Scale, 20.7
- Wechsler Memory Scale-Revised I/II, 5/0
- brain magnetic resonance imaging indicating multiple lacunar infarctions in the bilateral basal ganglions, including the striatum, and a 1.60 Z-score on

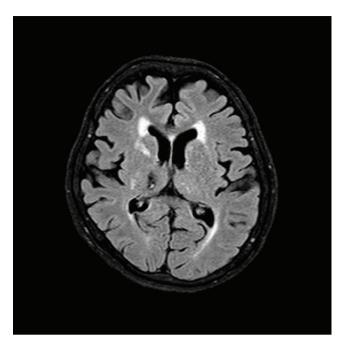


Figure 1 Head magnetic resonance imaging of the patient.

the voxel-based specific regional analysis system for Alzheimer's disease (Fig. 1)

 single-photon emission computed tomography with an easy Z-score imaging system analysis showing mild decrease of bilateral frontal blood perfusion.

The patient's primary diagnosis was finally changed to vascular dementia comorbid with depression. As she fell three times in the 4 days after full dose escalation of her antidepressant medication, we rediagnosed her primary condition as dementia. The acetylcholine inhibitor donepezil was administered, and sertraline was discontinued 7 weeks after she had begun taking it. We explained the off-label use of donepezil-donepezil can be potentially beneficial for patients with vascular dementia-and obtained oral consent from the patient and her family.⁴ Interestingly. the patient's depression seemed to respond well to donepezil. Her depressive mood, loss of energy, suicidal ideation, and psychomotor retardation disappeared after 3 weeks of 5-mg donepezil, but her cognitive impairment did not change. The patient provided her informed oral consent for this case report.

DISCUSSION

The present case suggests that anti-dementia drugs were an appropriate alternative treatment for depression in this patient with vascular dementia, although her first late-life depressive episode had responded well to an antidepressant. The differential response to pharmacotherapy in this case suggests that late-life depression may not be a simple prodromal symptom of dementia. However, it is not clear whether depression is an independent risk factor for dementia. Depression may be a very early symptom of dementia; depression and dementia might share common risk factors; or there might be no true association.3 This case may also support the reserve threshold theory, a prominent explanation of the mechanisms underlying the association between late-life depression and dementia.5 Reserve threshold theory holds that late-life depression injures neurons through a number of processes that lower cognitive reserve. This results in the early expression of cognitive impairment. Our case suggests that underlying cerebrovascular disease contributes to frontostriatal damage, and this damage may be associated with the development of mild cognitive impairment. Furthermore, late-life depression can increase cognitive impairment, thus leading to clinical dementia.

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REFERENCES

- 1 Alexopoulos GS, Bruce ML, Silbersweig D, Kalayam B, Stern E. Vascular depression: a new view of late-onset depression. *Dialogues Clin Neurosci* 1999; 1: 68–80.
- 2 Diniz BS, Butters MA, Albert SM, Dew MA, Reynolds CF III. Late-life depression and risk of vascular dementia and Alzhei-mer's disease: systematic review and meta-analysis of community-based cohort studies. *Br J Psychiatry* 2013; 202: 329–335.
- 3 Mitchell AJ. Depression as a risk factor for later dementia: a robust relationship? *Age Ageing* 2005; **34**: 207–209.
- 4 Malouf R, Birks J. Donepezil for vascular cognitive impairment. *Cochrane Database Syst Rev* 2004; **1**: CD004395.
- 5 Butters MA, Young JB, Lopez O et al. Pathways linking late-life depression to persistent cognitive impairment and dementia. Dialogues Clin Neurosci 2008; 10: 345–357.