Managing Depression in Cerebral Autosomal Dominant Arteriopathy With Subcortical Infarcts and Leukoencephalopathy (CADASIL): A Case Report

To the Editor: We present the case of a patient with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and major depressive disorder. This case highlights the importance of psychiatric evaluation and treatment for rare and deadly illnesses and the association between the brain areas that are affected in CADASIL and mood symptoms.

Case report. Mr A is a 55-year-old man with a known past medical history of multiple strokes, seizure, cognitive impairment (vascular type), major depressive disorder, posttraumatic stress disorder, diabetes mellitus, obstructive sleep apnea, hyperlipidemia, vitamin D deficiency, and obesity but no past psychiatry admission. He was admitted to the inpatient psychiatry unit for suicidal ideations. His history of strokes was due to an established diagnosis of CADASIL. Additionally, he had memory impairment and temporal sequence deficit; the latter was noticed recently.

At admission, Mr A reported depressed mood, anhedonia, insomnia, fatigue, loss of concentration, worthlessness, helplessness, hopelessness, and anxiety for 2 weeks. He denied any psychotic or manic symptoms. He was taking sertraline 100 mg for depression but was not under the care of a psychiatrist. Additionally, he was taking clopidogrel bisulfate 75 mg daily, lamotrigine 150 mg twice daily, and levetiracetam 1,500 mg 3 times daily. His Mini-Mental State Examination[1] score was 24 of 30, and his Montreal Cognitive Assessment[2] score was 18 of 30. His neurologic examination was significant for left hemianopsia and ataxia on tandem gait. Computed tomography and magnetic resonance imaging of the head showed no acute intracranial events. However, the imaging tests showed moderate to severe leukoencephalopathy reflective of chronic small vessel ischemia with multiple remote lacunar infarcts and larger infarcts involving the left thalamus extending to the caudate and globus pallidus and right temporal, parietal, and occipital lobes.

Mr A's sertraline dose was titrated to 200 mg daily. For cognitive impairment, donepezil was started and titrated to 10 mg daily. Mr A tolerated the medication change. He also benefited from milieu therapy. Shortly after admission, he showed improvement in his depressed mood, insomnia, loss of appetite, and suicidal ideation. No significant improvement in temporal sequence deficit or memory impairment was noticed.

CADASIL is a dominantly inherited small artery disease that causes multiple strokes, seizure, cognitive impairment in midlife (mean age at onset of 45 years old), and, consequently, death.[3] Other presenting symptoms of CADASIL can include migraine with aura, subcortical ischemic events, mood disturbances, and apathy.[3] Mutations in the *NOTCH3* gene on chromosome 19p13.1 were shown to be the etiology for CADASIL.[4] CADASIL is the most prevalent monogenic cerebral small vessel disease.[5] Although patients with CADASIL have been shown to suffer from emotional disturbances including depression, the emotional disturbances in these patients have not been completely understood.[6] As was shown in the present case, depression in these patients can be severe with suicidal ideations. The degree of depression can be associated with multiple infarcts including thalamic injuries, cognitive impairment, and caregiver burden.[6] It was reported in 2014 that quality of life in CADASIL patients was deteriorated and that caregiver burden was increased due to either depressive or nondepressive emotional disturbances.[6] Desmond et al[7] identified 105 CADASIL cases. They sought to explain the natural history of the disease. They found that 71 patients experienced stroke or transient ischemic attack, 52 patients had recurrent strokes, and 44 patients had dementia. Depression was an early symptom in 9 patients and was also associated in the progression of CADASIL in 13 patients.[7]

The main etiology of depression in CADASIL cannot be treated, but prophylactic measures such as screening for emotional disturbances, including depression, and psychopharmacologic intervention and counseling may assist in treating depression and improving quality of life in patients and their caregivers. Furthermore, since the risk for the disease can be assessed using genetic testing in those with a positive family history, regular prophylactic mental health support will definitely strengthen patients and their families with regard to depression and other possible mental health consequences.

References

1. Folstein MF, Folstein SE, McHugh PR. Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189–198.
2. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53(4):695–699.
3. Hervé D, Chabriat H. CADASIL. *J Geriatr Psychiatry Neurol*. 2010;23(4):269–276.
4. Joutel A, Corpechot C, Ducros A, et al. Notch3 mutations in cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), a mendelian condition causing stroke and vascular dementia. *Ann N Y Acad Sci*. 1997;826(1 Cerebrovascul):213–217.
5. Tan RY, Markus HS. Monogenic causes of stroke: now and the future. *J Neurol*. 2015;262(12):2601–2616.
6. Noh SM, Chung SJ, Kim KK, et al. Emotional disturbance in CADASIL: its impact on quality of life and caregiver burden. *Cerebrovasc Dis*. 2014;37(3):188–194.
7. Desmond DW, Moroney JT, Lynch T, et al. The natural history of CADASIL: a pooled analysis of previously published cases. *Stroke*. 1999;30(6):1230–1233.

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