CASE REPORT

Vascular Dementia Beyond Conventional Treatment: The Role of Neuroprotective Agents and Personalized Antiplatelet Therapy

Şükran Kaygısız^{1(ID)}

¹Ordu University, Faculty of Medicine, Department of Neurology, Ordu, Turkey,

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Abstract

Vascular dementia is a neurocognitive disorder caused by impaired cerebral blood flow due to vascular pathologies. Conventional pharmacological treatments often yield limited efficacy, necessitating adjunctive therapeutic strategies.

We report the case of a 75-year-old male patient with a history of hypertension and hyperlipidemia, presenting with progressive cognitive decline and psychiatric symptoms over four years. Initially misdiagnosed with a primary psychiatric disorder, the patient underwent various psychiatric treatments without significant improvement. Neurological evaluation revealed ischemic gliotic changes on magnetic resonance imaging (MRI), leading to a diagnosis of early-stage vascular dementia. Standard dementia treatment with donepezil and memantine was supplemented with citicoline, omega-3-6-9 fatty acids, and magnesium L-threonate. Furthermore, aspirin resistance testing revealed total resistance, prompting a switch to clopidogrel therapy. After four months, the patient showed cognitive improvement, with his Mini-Mental State Examination (MMSE) score increasing from 24 to 26.

This case highlights the importance of a comprehensive neurological and psychiatric evaluation in patients with cognitive decline. The integration of neuroprotective agents such as citicoline, omega fatty acids, and magnesium L-threonate may offer additional cognitive benefits in vascular dementia. Moreover, aspirin resistance should be considered in patients receiving antiplatelet therapy to optimize cerebrovascular protection.

Vascular dementia requires a multidisciplinary approach, including cognitive, psychiatric, and vascular risk management. Adjunctive neuroprotective therapies and personalized antiplatelet strategies may improve patient outcomes. Further research is needed to establish standardized protocols for managing vascular dementia with emerging therapeutic agents.

Keyword: Vascular dementia, Mini-Mental State Examination (MMSE), citicoline, magnesium L-threonate, aspirin resistance

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Address for correspondence/reprints:

Şükran Kaygısız

Telephone number: +90 (505) 925 39 04

E-mail: skrnkygsz52@gmail.com

INTRODUCTION

Vascular dementia arises from blockages in cerebral blood vessels and impaired cerebral blood flow. Vascular risk factors, notably hypertension and hyperlipidemia, are pivotal in its pathogenesis. These factors can lead to cerebrovascular damage, directly triggering vascular dementia. Moreover, they may elevate the risk of neurodegenerative diseases like Alzheimer's disease by promoting the accumulation of neurotoxic proteins in the brain (1).

Conventional pharmacological treatments for dementia often yield limited efficacy in vascular dementia cases. Consequently, adjunctive therapies such as citicoline, omega-3 fatty acids, and magnesium L-threonate which effectively crosses the blood-brain barrier—are employed to enhance treatment outcomes.

In neurodegenerative diseases, psychiatric symptoms can precede radiological findings due to underlying organic causes. Therefore, a comprehensive evaluation is essential before diagnosing psychiatric disorders, ensuring that organic etiologies are excluded. Aspirin resistance denotes the failure of acetylsalicylic acid to exert its intended antiplatelet effect. The prevalence of aspirin resistance varies widely, ranging from 5.5% to 60%, depending on the testing method used (2). Given this variability, routine testing for aspirin resistance is not universally recommended before initiating therapy. Instead, clinicians should be aware of factors that may impair aspirin function, ensure appropriate dosing, and optimize patient compliance (2).

This case involves a male patient with a history of hypertension and hyperlipidemia who has exhibited cognitive and psychiatric symptoms in recent years. These vascular risk factors likely contribute to his cognitive decline, underscoring the importance of managing such modifiable risks to potentially prevent or slow the progression of dementia.

CASE 1

A 75-year-old male patient, a graduate of an educational institute, operated a bagel bakery for eight years but had to close it due to financial difficulties five years ago. Over the past four years, he has experienced episodes of staring spells, social withdrawal, reduced communication with family members, and a preference for solitude. While he can still perform basic arithmetic, he struggles with more complex calculations. He has become increasingly emotional and forgetful.

He frequently engages in verbal disputes with others and experiences sudden explosive anger episodes, followed by immediate remorse, in the mosque setting, which is typically a congested area Previously, he enjoyed reading novels, daily newspapers, and solving puzzles; however, he stopped reading two years ago due to comprehension difficulties. Over the past year, he has also experienced difficulties with spatial orientation.

A brain MRI performed at an external center four years ago reported: "Millimetric ischemic gliotic foci observed in bilateral centrum semiovale regions." These ischemic gliotic foci were attributed to the patient's history of hyperlipidemia. and hypertension Consequently, he was prescribed antihypertensive medication and 80 mg of acetylsalicylic acid, along with dietary and exercise recommendations for hyperlipidemia management.

His symptoms of forgetfulness, anxiety, and emotionality heightened were initially considered psychological, and antidepressant treatment was initiated. However, as his complaints progressively worsened, more aggressive psychiatric treatments were administered. Recently, he became unable to find his way home after visiting a local market, prompting another hospital visit. A psychiatric

specialist referred him to the neurology department for further evaluation.

The patient has a medical history of hypertension and hyperlipidemia, with stable blood pressure around 100/60 mmHg under 10 mg of perindopril. He is not on any medication for hyperlipidemia. One year ago, he underwent surgery for urethral stricture. He has no history of smoking, alcohol consumption, or other known medical conditions.

Neurological Examination and Imaging Findings

Neurological examination revealed а diminished left nasolabial fold. Muscle strength was assessed as +4/5 in the left upper extremity and -5/5 in the left lower extremity. Deep tendon reflexes were normoactive in the bilateral upper extremities but hyperactive in the bilateral lower extremities. The MMSE score was 25. The patient was unable to perform serial subtraction by sevens, failed to draw a cube, and inaccurately reproduced the intersecting pentagon figure, drawing only four sides in one of the pentagons. His recall ability was partial.

Brain MRI showed hyperintense areas in the FLAIR sequence within both lateral ventricles, anterior horn regions, bilateral centrum semiovale, and internal watershed areas. T2weighted imaging revealed widespread Virchow-Robin spaces in the bilateral centrum semiovale, thalamus, and basal ganglia. Carotid MR angiography and cervical MRI were evaluated as normal.

Laboratory tests indicated an LDL level of 147 mg/dL (normal range: <100 mg/dL) and an HbA1c level of 6.1% (normal range: <5.7%). The vasculitis panel and other blood tests were within normal limits. Given the clinical presentation, the patient was diagnosed with early-stage vascular dementia. His acetylsalicylic acid dose was increased to 150 mg; however, aspirin resistance testing later revealed total resistance. Consequently, he was switched to clopidogrel therapy. Cardiological evaluation found no pathological abnormalities. The patient was consulted with psychiatry, and his psychiatric medications were discontinued. Instead, he was started on fluoxetine (20 mg), donepezil, memantine, and Ginkgo biloba, with gradual dose adjustments over three months. At follow-up, his MMSE score was 24. Consequently, fluoxetine was increased to 40 mg in the morning, and magnesium L-threonate (1x1) and a citicoline + omega-3-6-9 complex were introduced. After four months of followup, the patient's MMSE score improved to 26, and he was able to correctly draw both the cube intersecting pentagons. and The patient continues his current treatment and remains under follow-up at the neurology outpatient clinic.

DISCUSSION

Vascular dementia is a progressive neurological disorder characterized by cognitive decline

resulting from cerebrovascular disease. It is closely associated with vascular risk factors such as hypertension, hyperlipidemia, and diabetes mellitus (3). While current pharmacological treatments aim to slow disease progression and manage symptoms, their overall effectiveness remains limited. Consequently, research into novel therapeutic approaches, particularly neuroprotective strategies, has gained increasing attention.

The Need for Neuroprotective Approaches

Traditional treatments for vascular dementia. including cholinesterase inhibitors (e.g., donepezil) and N-methyl-D-aspartate (NMDA) receptor antagonists (e.g., memantine), primarily focus on symptomatic relief rather than addressing the underlying vascular pathology (4). However, emerging evidence suggests that neuroprotective agents such as citicoline, omega 3 fatty acids, and magnesium L threonate may offer additional benefits by promoting neuronal repair, enhancing synaptic plasticity, and improving cerebral blood flow (4). Citicoline (CDP choline), a precursor of phosphatidylcholine (a key component of cell membranes) has been shown to enhance acetylcholine production. It supports neuronal repair mechanisms and increases neurotransmitter availability, which can improve cognitive function. Recent studies demonstrated have that citicoline supplementation leads to improvements in memory, attention, and overall cognitive

performance in individuals with vascular dementia and mild cognitive impairment (4).

Similarly, omega 3 fatty acids (particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)) are essential for maintaining neuronal integrity and reducing neuroinflammation. These fatty acids have been linked to improved cognitive function and a lower risk of dementia (5). In addition to their neuroprotective properties, omega 3 fatty acids have been found to alleviate psychiatric symptoms, such as depression and anxiety, which are frequently observed in vascular dementia patients. Given that psychiatric symptoms often precede cognitive impairment, integrating omega 3 supplementation into treatment plans may help improve both neurological and psychiatric outcomes.

Magnesium L threonate is another promising neuroprotective agent due to its ability to effectively cross the blood brain barrier. vital role Magnesium plays a in neurotransmission, synaptic plasticity, and neuroprotection. Studies have suggested that magnesium L threonate supplementation can improve learning, working memory, and overall cognitive function (6). Given that magnesium deficiency has been implicated in the progression of neurodegenerative disorders, targeted magnesium supplementation may be beneficial in the management of vascular dementia.

The Role of Psychiatric Symptoms in Vascular Dementia

One of the critical aspects of vascular dementia that is often overlooked is the presence of psychiatric symptoms. Depression, anxiety, irritability, emotional dysregulation, and even psychotic features can emerge in the early stages of the disease, sometimes preceding cognitive decline (7). These symptoms can complicate diagnosis, as they are frequently misattributed to primary psychiatric disorders. In the case discussed, the patient initially received multiple psychiatric treatments before being referred for neurological evaluation, which underscores the need for a thorough assessment of psychiatric symptoms in older adults. Underlying organic causes should be ruled out before diagnosing a primary psychiatric disorder.

Fluoxetine, a selective serotonin reuptake inhibitor (SSRI), was included in this patient's treatment regimen due to its role in neuroregeneration and axonal sprouting. SSRIs have been found to exert neuroprotective effects by enhancing brain derived neurotrophic factor (BDNF) levels, which may support cognitive function in dementia patients (8). The combination of fluoxetine. donepezil, memantine, and Ginkgo biloba contributed to improved cognitive function, as evidenced by the patient's increasing MMSE score over time. This case underscores the importance of addressing both cognitive and psychiatric symptoms in vascular dementia management.

Aspirin Resistance and Its Clinical Implications

Aspirin resistance presents a significant challenge in the management of vascular dementia, given that antiplatelet therapy plays a crucial role in preventing further cerebrovascular events. Aspirin works by irreversibly inhibiting cyclooxygenase 1 (COX 1), thereby reducing platelet aggregation. However, some patients exhibit resistance to aspirin-meaning that it fails to achieve the expected antiplatelet effect—which can increase the risk of recurrent ischemic events (9).

In the discussed case, aspirin resistance testing revealed complete resistance, necessitating a switch to clopidogrel therapy. Clopidogrel, a P2Y12 receptor antagonist, inhibits platelet activation through a different mechanism and is thus an effective alternative for patients with Given the clinical aspirin resistance. implications of aspirin resistance, routine screening may be beneficial in high risk patients to ensure that antiplatelet therapy is tailored to individual needs. Several factors contribute to aspirin resistance, including genetic polymorphisms, drug interactions, and metabolic differences. Genetic variations in cyclooxygenase enzymes or platelet receptors can alter aspirin's effectiveness, while the concomitant use of nonsteroidal antiinflammatory drugs (NSAIDs) may interfere with its mechanism of action. Identifying these factors through genetic and pharmacokinetic testing could help optimize treatment strategies for vascular dementia patients.

The Importance of a Multidisciplinary Approach

The management of vascular dementia necessitates a multidisciplinary approach that integrates neurology, psychiatry, cardiology, and geriatric medicine. This case highlights the need for comprehensive diagnostic workups (including neuroimaging, cognitive assessments, psychiatric evaluations, and pharmacogenetic testing) to develop personalized treatment strategies. In addition to pharmacological interventions, lifestyle modifications such as dietary changes, physical exercise, and cognitive rehabilitation should be emphasized. Regular physical activity has been shown to enhance cerebral blood flow, reduce vascular risk factors, and improve cognitive function. Similarly, a Mediterranean diet rich in omega 3 fatty acids, antioxidants, and polyphenols may help slow cognitive decline in patients with vascular dementia (5).

Future Directions in Vascular Dementia Treatment

Despite recent advances in vascular dementia research, there remains a need for more targeted therapies that address the underlying vascular pathology and neurodegenerative processes (4).

Future studies should explore the potential of combination therapies that incorporate anti-inflammatory neuroprotective agents, compounds, and personalized antiplatelet (6). Additionally, investigating strategies biomarkers for early diagnosis and treatment could help refine therapeutic response approaches (9). Emerging treatments—such as stem cell therapy, neurostimulation techniques (e.g., transcranial magnetic stimulation), and novel pharmacological agents targeting neuroinflammation and oxidative stress-may provide new avenues for managing vascular dementia (5). As research progresses, a more personalized approach to treatment is likely to emerge, ultimately improving patient outcomes and quality of life (8).

CONCLUSION

In summary, this case highlights the complexity of vascular dementia management and the importance of a multidisciplinary approach. While conventional treatments provide limited benefits, integrating neuroprotective agents such as citicoline, omega-3 fatty acids, and magnesium L-threonate may enhance cognitive function and slow disease progression. Psychiatric symptoms should not be overlooked, as they can significantly impact disease course and treatment outcomes. Additionally, aspirin resistance testing may help optimize antiplatelet therapy, reducing the risk of further cerebrovascular events. Future research should focus on personalized treatment strategies that address both the vascular and neurodegenerative aspects of the disease.

Ethics Committee Approval: The presented study is qualitative and consent was obtained by giving information about the study by one-toone interviews with the subjects who agreed to participate. The study was carried out by paying attention to the Declaration of Helsinki.

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