VASCULAR DEMENTIA

Key Concepts

- Definition of vascular dementia
- Pathophysiology of vascular dementia
- Imaging studies of vascular dementia
- Treatment of vascular dementia

Abstract:
Vascular dementia is a heterogeneous entity with a large clinicopathological spectrum that has been classically linked to cortical and subcortical ischemic changes resulting from systemic, cardiac, or local large- or small-vessel disease occlusion. Thus, the diagnosis of vascular dementia is usually made on the basis of clinical, neuroimaging, or neuropathological evidence of cerebral ischemia in the presence of progressive cognitive decline.

Background
Vascular dementia is a heterogeneous entity with a large clinicopathological spectrum that has been classically linked to cortical and subcortical ischemic changes resulting from systemic, cardiac, or local large- or small-vessel disease occlusion. Thus, the diagnosis of vascular dementia is usually made on the basis of clinical, neuroimaging, or neuropathological evidence of cerebral ischemia in the presence of progressive cognitive decline.

Pathophysiology
Vascular dementia results from brain injury caused by stroke and cerebral ischemia. Single ischemic or thromboembolic infarcts occurring in strategic areas of the dominant hemisphere (e.g., angular gyri, mediodorsal thalamus, anterior thalamus) may cause a dementia-like syndrome without the involvement of large volumes of cerebral matter. In general, volume of tissue loss is a poor predictor of the severity of the cognitive impairment.

More commonly, progressive cognitive deficits and dementia can result from multiple temporally staggered small cerebral infarcts. Frontal subcortical regions supplied by small penetrating arterioles may be especially prone to degenerative changes in patients with poorly controlled hypertension, diabetes mellitus, or both.
A less common cause of vascular dementia is global hypoxic-ischemic injury (eg, following cardiac arrest). Irreversible cognitive impairment is frequently observed following coronary bypass surgery.

Whether chronic cerebral ischemia associated with carotid artery stenosis (CAS) may alter cognitive function has not been conclusively demonstrated and remains a controversial concept. Neuropsychometric evaluation of patients undergoing carotid endarterectomy has not conclusively shown cognitive impairment or reductions in the probability of developing dementia in the long term.

An ill-understood form of vascular dementia is Binswanger encephalopathy. Postmortem, myelin loss is observed and is most prominent in the hemispheric deep white matter. Axonal drop out is also observed with little or no signs of inflammation. Neuroimaging shows decreased white matter density on CT scanning and decreased white matter intensity on T1-weighed MRI. Frequently, but not invariably, lacunar strokes are also observed.

Dementia associated with cerebrovascular disease is also observed in a rare genetic condition, ie, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). Affected patients often present with migraines with aura. Recurrent strokes start when the patients are aged 30-50 years. Multiple lacunar infarcts, mainly in the frontal white matter and basal ganglia, lead to progressive cognitive decline and finally dementia. However, cognitive decline is thought to begin even before strokes occur, suggesting that chronic cerebral hypoperfusion in the absence of overt stroke might be sufficient to cause significant neuronal circuit disruption.

History
Criteria for the diagnosis of dementia require impairment in memory and at least 1 other cognitive domain (eg, orientation, language, praxis, executive functions, visuospatial abilities). These should be serious enough to affect activities of daily living and be consistently present to distinguish dementia from episodic impairments of consciousness such as delirium.

Currently, several sets of diagnostic criteria for vascular dementia exist. This list summarizes the main common criteria.
- Vascular risk factors such as hypertension, coronary disease, and diabetes mellitus
- Specific evidence of cerebrovascular disease, eg, strokes and transient ischemic attacks: The cerebrovascular insult should proceed (by no more than 3 months) or coincide with the onset or worsening of cognitive abnormalities.
- Neuroimaging evidence of strokes
- Lateralizing neurologic signs
- Psychiatric disturbances (e.g., emotional lability, depression, apathy)

Depression is a common comorbidity in patients with cerebrovascular disease and vascular dementia.

Medications should be reviewed because of the potential of drugs to interfere with alertness and cognition.

Differences between the cognitive disturbances in vascular dementia and Alzheimer disease are of limited value in discriminating vascular dementia from Alzheimer disease in a clinical setting.
Vascular dementia is thought to be associated with less significant memory dysfunction than Alzheimer disease.

Frontal dysfunction due to widespread involvement of subcortical structures in vascular dementia is thought to lead to a dysexecutive syndrome with abulia and apathy.

A cognitively impaired patient with vascular risks factors but no history of cerebrovascular disease is most likely to have Alzheimer disease. Patients with dementia and vascular disease frequently have mixed pathology (ie, both Alzheimer disease and vascular dementia).

**Physical Examination**
The physical examination should be focused on the cardiovascular system and neurologic localizing signs.

- The temporal arteries may show decreased pulsatility, local tenderness, and thickening associated with giant cell arteritis.
- Funduscopic examination provides important information regarding end-organ effects of hypertension and diabetes mellitus.
- Cardiac auscultation may detect rhythmic and valvular abnormalities.
- Spasticity, hemiparesis, visual field defects, pseudobulbar palsy, and extrapyramidal signs confirm focal pathology.

**Causes**
Vascular dementia and cerebrovascular disease share risk factors, including age, male sex, diabetes mellitus, hypertension, cardiomyopathy, and possibly homocysteine levels.

- So far, no relationship between cholesterol, serum lipoproteins, and the risk of vascular dementia is clearly indicated.

- Evidence for tobacco consumption as a risk factor for vascular dementia is conflicting. However, a multiethnic, population-based study published in 2010 suggested that the brain is not immune to long-term consequences of heavy smoking.

- Limited alcohol consumption may be protective

**Differential Diagnoses**
- Alzheimer Disease Imaging
- Cortical Basal Ganglionic Degeneration
- Dementia in Motor Neuron Disease
- Dementia With Lewy Bodies
- Frontotemporal Dementia and Frontotemporal Lobar Degeneration

**Laboratory Studies**
All patients with dementia should have laboratory testing to rule out reversible causes of dementia. CBC, electrolytes, thyroid-stimulating hormone (TSH), folate, and vitamin B-12 levels should be obtained. The American Academy of Neurology no longer recommends syphilis screening in the routine evaluation of dementia if patients come from geographic regions with a very low base rate of syphilis. In specific cases, screening for syphilis is indicated.

If the clinician has reason to suspect an angiitis affecting cerebral vessels, then an erythrocyte sedimentation rate (ESR) and specific panels may be ordered.

**Imaging Studies**
Patients with newly diagnosed dementia undergo neuroimaging studies to rule out treatable causes of dementia and to aid the differential diagnosis.
Either CT scanning or MRI of the head should be performed.

In patients with vascular dementia, multiple cortical and more commonly subcortical, infarcts or single strokes affecting the thalamus, angular gyrus, and the territory supplied by the anterior cerebral arteries are observed.

Decreased white matter density (on CT scanning) or decreased T1 or increased T2 signal intensities (on MRI) are associated with dementia. Multiple pathologies, including small vessel disease and decreased integrity of the blood-brain barrier, have been associated with these findings.

Measurement of cerebral blood flow using single photon emission computerized tomography (SPECT) or positron emission tomography (PET) scanning is not recommended for diagnostic purposes.

**Medical Care**

The treatment of vascular dementia is symptomatic. Behavioral and psychiatric disturbances such as agitation, depression, and psychosis are common. Cerebrovascular disease should be treated by an internist and/or a neurologist familiar with the management of cerebrovascular disease.

- Established protocols for the evaluation and treatment of stroke are available. The individual approach combines a vascular risk factor modification and various treatments addressing the specific subtypes of stroke, such as antiplatelet drugs for the prevention of cerebral infarction in large and small artery diseases of the brain, carotid endarterectomy or stenting for tight carotid artery stenosis, and oral anticoagulants for the prevention of cardiac emboli.
- The presence of a rapidly progressive dementia and multiple strokes in a young patient may indicate uncommon causes of stroke such as CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) or angitis. If suspected on clinical grounds, these conditions should be excluded with the appropriate testing procedures (ie, skin biopsy, cerebral angiography). The decision to use anticoagulation in patients with vascular disease and dementia is particularly challenging because of the increased risk of falls and potential noncompliance in this group.
- Patients with vascular dementia are prominently affected by depression and emotional incontinence. Both conditions respond well to treatment with serotonin reuptake inhibitors.
- Patients with agitation may respond to environmental modification. Pharmacologic treatment can be useful in controlling agitation through sedation.

**Medication Summary**

No approved pharmacologic treatment exists for vascular dementia.

Risk factors for cerebrovascular disease should be treated when present.

Retrospective data indicate that normotensive patients with vascular dementia may have greater cognitive decline than hypertensive patients. This finding, as well as the known loss of cerebral blood flow autoregulation in chronic hypertension and cerebrovascular disease, should temper overenthusiastic attempts to normalize the blood pressure in
patients with vascular dementia.

Treatment with antiplatelet agents may be initiated as indicated by the nature of the patient’s underlying vascular pathology.

Cholinesterase inhibitors, which include donepezil, rivastigmine, and galantamine, have proven symptomatic efficacy in Alzheimer disease and may also have a role in the treatment of vascular dementia according to the findings of limited studies. Presently, their use may have some justification given the prevalence of dementia with mixed pathology.

**Prognosis**
The rate of progression of cognitive impairment in vascular dementia is variable; some patients progress at a slower rate than patients with Alzheimer disease. The mortality rate, however, is higher in patients with vascular dementia than in patients with Alzheimer disease, with 50% of patients with vascular dementia not living longer than 4 years. While waiting for effective drug therapies and first-level evidence data, healthcare professionals should be encouraged to improve early diagnosis of cognitive impairment and activate control strategies against vascular disease and unhealthy lifestyle habits.

**REFERENCES**