Stroke and dementia

Article *in* Neurological Research · November 2009

DOI: 10.1179/016164109X12445505689643 · Source: PubMed

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Stroke and dementia

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Objective: *The current review covers causes and risk factors of vascular dementia, including single infarct, multi-infarct and cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy. Comparisons and distinctions are made between vascular dementia and Alzheimer's dementia, including shared vascular features and risk factors, differential diagnosis based on presenting history, neuropsychological testing results and neuroimaging findings. Neuropsychological findings associated with vascular dementia are discussed, and efforts towards stroke prevention and limiting the recurrence of stroke, as well as emerging treatment possibilities for cognitive decline associated with vascular dementia, are presented.*

Methods: *A PubMed-based literature review was performed to acquire recent peer-reviewed publications on vascular dementia.*

Results: *Stroke is one of the leading causes of disability, dementia and death. Within the USA, roughly 660,000 persons will experience a stroke each year. Although many individuals go on to demonstrate substantial improvement and recovery following stroke, a substantial percentage show residual effects including dementia. Vascular dementia has variable causes and manifestations, and research is revealing increasingly more common ground between vascular dementia and Alzheimer's dementia. However, vascular dementia often remains clinically distinct from Alzheimer's dementia, and profiles of neuropsychological impairment can be used to differentiate vascular dementia from the more common Alzheimer's dementia with some success.*

Conclusion: *Vascular dementia causes dependence and disability. Most stroke survivors show improvement, but many develop dementia. Understanding for vascular dementia has recently improved, leading to improved treatment planning. Further research, especially on treatment for vascular dementia, is greatly needed.* [Neurol Res 2009; **31**: 824–831]

Keywords: Cognition; dementia; neuropsychological; stroke; vascular

INTRODUCTION

Stroke is the second most common cause of dementia and the third most common cause of death in developed countries[1]. Within a population of roughly one million persons, some 2400 will suffer a stroke each year. Of those persons suffering stroke, less than 50% will return to independent living during the following year[1]. Even among those who regain functional independence, many stroke patients continue to manifest significant deficits, limitations and changes in their cognitive functioning and behavior. These deficits, limitations and changes can result in salient negative consequences in an individual's professional and family life[1]. As such, stroke is one of the leading causes of disability, and experiencing a stroke results in a two-fold increase in risk for dementia[1]. An increased risk of dementia following stroke has also been found to be associated with lower education, older age, pre-stroke cognitive decline insufficient to be described as dementia, pre-stroke dependency upon others, diabetes mellitus, myocardial infarction, atrial fibrillation, epileptic seizures, sepsis, cardiac arrhythmias, congestive heart failure, global cerebral atrophy and medial temporal lobe atrophy, and white matter changes[1]. Those factors associated with stroke which are predictive of resultant dementia include the severity of stroke, its cause and location, and recurrent stroke[1].

The two most common causes of cognitive impairment and dementia include Alzheimer's dementia and vascular dementia. Alzheimer's dementia, a neurodegenerative disorder, is the more prevalent of the two. However, vascular dementia is nonetheless seen as the causal agent in among up to 30% of demented individuals. Vascular dementia typically occurs among the elderly, but it can affect younger patients as well[2]. It is estimated that roughly seven million Americans suffer from dementia, with some 4.5 million of those persons suffering from Alzheimer's dementia[3]. Individuals with vascular dementia often manifest cognitive impairment and dementia, behavioral changes and mood disorder, and specific neurological symptoms[2].

Differentiating between the two dementias for diagnostic purposes is not always a straightforward or simple

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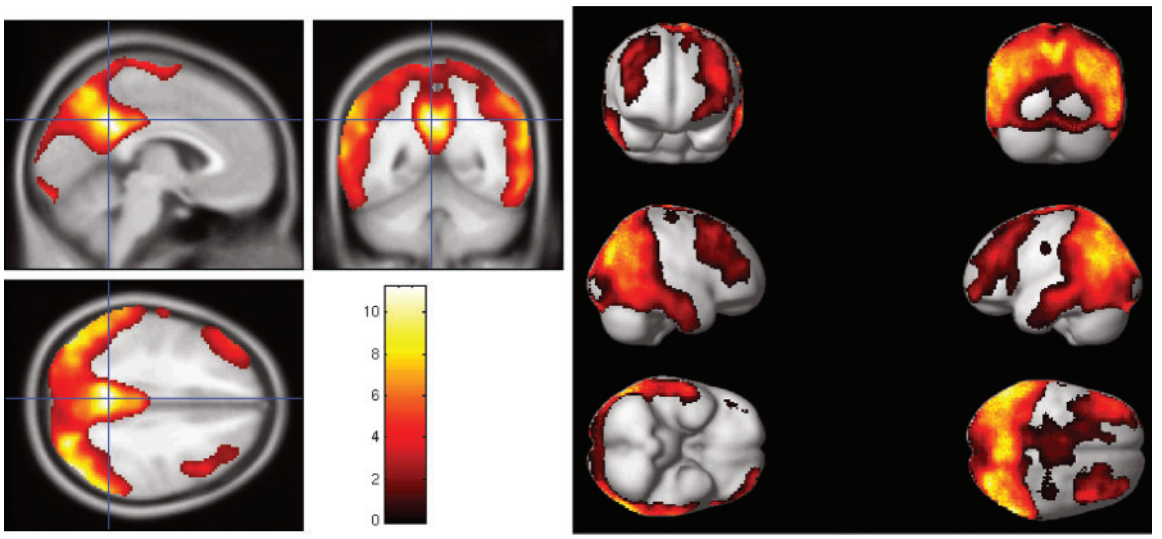

Figure 1: This subject is a 49-year-old woman with severe Alzheimer's dementia who shows statistically significantly abnormal hypoperfusion in parietal and temporal regions on 18FDG PET imaging. The colored scale shows the number of standard deviations from the mean with yellow, indicating the greatest hypoperfusion compared to normal controls

procedure. However, several characteristics common to either Alzheimer's dementia or vascular dementia can help make this distinction[4] (*Table 1*). The clinician should bear in mind that these are not hard and fast delineations, and some overlap and blending of symptom manifestation across the two diagnoses is occasionally seen.

Metabolic differences are also seen among individuals with Alzheimer's dementia and vascular dementia. Specifically, individuals with Alzheimer's dementia most often demonstrate hypoperfusion within temporal and parietal areas compared to normal controls (*Figure 1*). There can be a predominance in temporal (with disturbances in language more pronounced) or in parietal (with apraxia) lobes. In contrast, individuals with vascular-related dementia often demonstrate multiple areas of hypoperfusion within the superficial and deep gray matter.

Recent studies have changed the way we think about dementia, particularly Alzheimer's dementia and vascular dementia. Whereas it was common in the past to consider causes of dementia separately within a given individual, it has recently been shown that patients with cerebrovascular disease show a greater propensity to develop Alzheimer's dementia[3], and up to 60% of persons with presumed Alzheimer's dementia also have vascular dementia[1]. The concurrence of Alzheimer's dementia and vascular dementia is attracting more attention among researchers and clinicians. Considering the effect of cerebral vascular disease on Alzheimer's dementia, as found among past neuropathic studies including the Nun study and the MRC-FAS study, cerebrovascular disease may be associated with up to 80% of dementia found in old age[3].

There now appears to be considerable overlap between the risk factors and pathology of Alzheimer's dementia and vascular dementia[5]. Whereas the early cognitive findings in Alzheimer's dementia and vascular dementia show different patterns, substantial concurrence is found between pathological and clinical features, and longitudinal studies suggest strong associations between the role vascular factors play in the development of both Alzheimer's dementia and vascular dementia[5]. Neuropathic studies in Alzheimer's dementia further bolster the importance of vascular alterations in the disease's pathogenesis by revealing

Table 1: Differentiation of Alzheimer's dementia from vascular dementia

Characteristic	Alzheimer's dementia	Vascular dementia
Onset	Gradual	Sudden or gradual
Progression	Constant decline	Slow, stepwise decline
Neurological findings	None or subtle	Focal deficits
Memory	Early and pronounced deficit	Mild impairment
Executive dysfunction	Late appearance	Early and pronounced
Dementia type	Cortical	Often subcortical
Neuroimaging	Hippocampal atrophy	White matter lesions, infarcts
Gait	Typically normal	Early difficulties
Cardiovascular history	Less common	TIA, CVA, vascular risk factors

Modified from Gustavo[4]. TIA: transient ischemic attack; CVA: cerebral vascular accident.

concurrent vascular and degenerative changes[6]. Furthermore, recent research has revealed similar hemodynamic alterations in both Alzheimer's dementia and vascular dementia, and ultrasound analysis of cerebral hemodynamics has been shown to be unable to differentiate between the two causes of dementia[6].

Nonetheless, Alzheimer's dementia and vascular dementia often present with clinically different manifestations. Specifically, individuals with vascular dementia usually demonstrate less severe memory difficulties in comparison to other cognitive limitations. This apparent relative preservation of memory functioning among patients with vascular dementia may lead to the under diagnosis of dementia and failure to fully recognize significant cognitive decline among this population[3].

VASCULAR DEMENTIA

Numerous causal factors appear to participate in the genesis of diverse manifestations of vascular dementia[5]. As such, the construct of vascular dementia is complex, making the establishment and application of strict definitional criteria difficult[7]. As a category, vascular dementia encompasses several clinical syndromes, including subcortical lacunar infarcts, subcortical white matter lesions and multiple cortical lesions[8]. Vascular dementia can also result from a variety of causes. Cognitive impairment associated with vascular dementia is also variable and may include cortical manifestations and subcortical elements[8].

From a strict definitional standpoint, the diagnosis of dementia requires the presence of significant memory impairment in the context of other cognitive difficulties, including at least one of the following: aphasia, apraxia, agnosia or executive functioning. These difficulties must constitute significant impairment in an individual's functioning. Given the variability inherent in vascular related cognitive decline and vascular dementia, patients may present with many different cognitive impairment profiles at various levels of severity. Oftentimes, their difficulties are not characterized by primary memory impairment, though impaired memory is often present[2]. Furthermore, the formal diagnosis of vascular dementia requires that the onset of cognitive difficulties be related to demonstrable vascular changes[8]. This may be difficult to establish given the sometimes insidious onset of cognitive decline associated vascular changes, or the unavailability of sufficient neuroimaging techniques.

Vascular dementia does not always present in a pure form. Often times, the patient presents with a mixed dementia and demonstrates cognitive decline attributable to Alzheimer's dementia or other ideologies as well as vascular related changes[2]. Even if vascular dementia can be considered pure in form, it may arise from different types of events. Specifically, the patient may manifest symptoms of dementia following a single infarct, multiple infarcts or small vessel disease[2].

A single infarct in a functionally critical area or subcortical site may result in dementia in and of itself. For example, single lesions within the distribution of the carotid, anterior, middle and posterior cerebral arteries can produce syndromes of dementia with various neurological and neurobehavioral symptoms[2]. Dementia resulting from multiple infarcts is also often the cause of vascular dementia. In this case, the dementia is attributable to multiple ischemic infarcts, typically within the large vessels, which disrupt cortical and subcortical areas[2]. The patient typically manifests a pattern of deficits associated with the infarcted regions rather than a more global pattern of dysfunction as is often seen among patients with Alzheimer's dementia.

SMALL VESSEL DISEASE INDUCED VASCULAR DEMENTIA

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a generalized a small vessel disease caused by a mutation in the NOTCH3 gene and manifests clinically with recurrent stroke and associated cognitive decline[9]. It most often occurs in periventricular white matter, deep white matter and regions of the basal ganglia (*Figure 2*). The natural course is variable with transient ischemic attacks and strokes as the main characterizing sequelae[10]. Up to one-fifth of individuals with CADASIL show mood disorders, most prominently depression or anxiety. Up to one-third of individuals with CADASIL manifest migraine headache[10]. The cumulative effect of these recurrent strokes and transient ischemic attacks is an insidious cognitive decline leading to subcortical dementia, the process of which is not well understood[10]

Cognitive changes have been noted in patients with CADASIL even before transient ischemic attack or stroke[10]. Specifically, researchers have noted declines in working memory and executive functioning before stroke. Following stroke, patients with CADASIL manifest difficulties with mental processing speed and visual spatial ability[10]. Once patients evidence dementia, multiple cognitive deficits emerge, including deficits in verbal functioning and verbal episodic memory, as well as problems with motor speed. However, episodic memory may be reasonably well preserved, even in the later stages of the disease[10]. Cognitive decline appears to begin even before the individual with CADASIL experiences transient ischemic attack or stroke[10].

The cognitive skills of individuals with CADASIL were further investigated in a sample of patients aged 35–73 years[11]. Results showed that all of the younger patients manifested executive dysfunction, and the majority showed memory difficulties (70%) and attentional problems (69%). Visual spatial reasoning was found to decline with age, particularly after age 60 years[11]. Approximately one-fourth of patients studied manifested dementia, with 75% being over 60 years of age; patients over 60 years of age manifested significant difficulties in all cognitive areas. No significant correlation was found between the presence of dementia and number of ischemic events. Finally, difficulties with memory were best described as

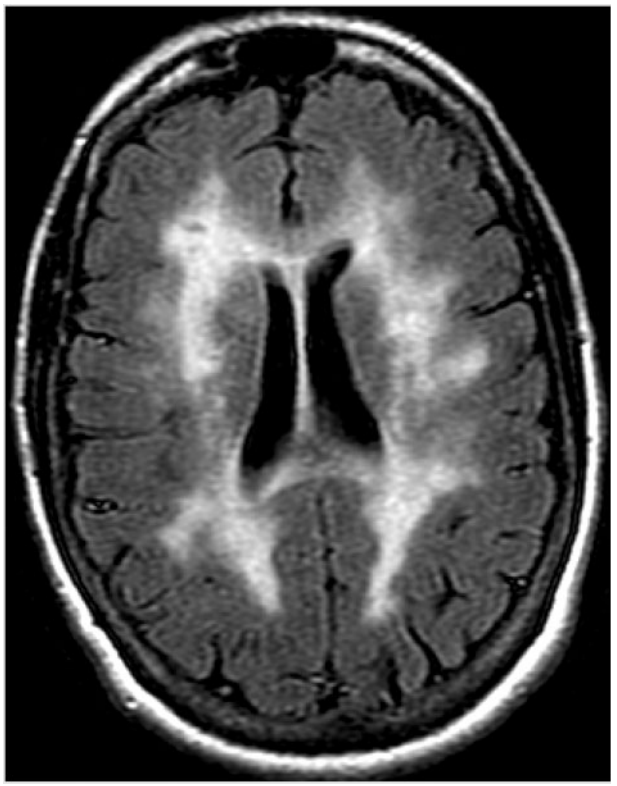

Figure 2: Magnetic resonance FLAIR in a patient with CADASIL showing typical demyelination involving the temporal pole and external capsule

problems with memory retrieval, whereas encoding abilities appeared relatively preserved[11].

Other researchers have examined the relationship between magnetic resonance imaging (MRI) and neuropsychological testing results among individuals with CADASIL[9]. Focusing on white matter hyperintensities, infarct lesion load and microbleeds, investigators noted that cognitive dysfunction was independently associated with MRI determined infarct lesion load[9]. However, amounts of white matter hyperintensities lesions and microbleeds were not highly correlated with cognitive dysfunction. The authors note the importance of lacunar infarct lesion load as an MRI parameter predictive of cognitive dysfunction in CADASIL[9].

Further neuroimaging studies include the use of diffusion tensor imaging as an investigatory technique in CADASIL. Authors have reported significant correlations between performance on measures of executive functioning and diffusion tensor imaging in both normal appearing gray matter and white matter[12]. The strongest association was between executive functioning and gray matter within the thalamus, even after controlling for gender, age and T2 lesion load. The authors concluded that abnormalities within normal appearing white matter and deep gray matter can be found among non-demented individuals with CADASIL and that diffusion tensor imaging measurements are highly correlated with, and useful in predicting, deficits in executive functioning[12].

Finally, both high-resolution MRI and single photon emission computed tomography imaging are reported in patients with CADASIL. However, some researchers have noted the absence of significant correlates between functional neuroimaging and a patient's cognitive performance, or patient and vascular risk histories[13]. Specifically, the authors indicated that, in their investigation, the subject least affected from a neuroradiological standpoint met criteria for dementia, whereas the most severely neuroradiologically affected subject manifested the best clinical and cognitive performance[13]. The authors concluded that conventional structural and functional neuroimaging, although important in the diagnosis of CADASIL, may be insensitive to cognitive decline. Instead, they recommended comprehensive neuropsychological evaluation, particularly for assessment of outcome parameters for various therapeutic measures[13].

NEUROPSYCHOLOGICAL CHANGES FOLLOWING STROKE

The neuropsychological profile of individuals with vascular dementia presents with more variability than those with Alzheimer's dementia. Researchers have looked for a distinct profile indicative of vascular dementia, and some have reported a higher percentage of deficits in executive functioning with more preserved episodic memory as compared to individuals with Alzheimer's dementia. Among individuals with Alzheimer's dementia, the occurrence of dementia has been found to be well correlated with the level of neurofibrillary pathology, but symptoms of dementia were unrelated to severity of cerebrovascular disease as determined by autopsy[14]. The more predictable and uniform presentation of cognitive deficits among persons with Alzheimer's dementia allows for high sensitivity and specificity of diagnoses based on the blind evaluation of neuropsychological test results. The profile of cognitive impairment among individuals with vascular dementia is highly variable and neuropsychological evaluation by trained professionals can be beneficial in differential diagnosis for these persons[14].

The finding that individuals with vascular dementia typically do better on memory testing and worse on assessment of executive functioning as compared to those with Alzheimer's dementia has spurred some researchers to investigate if a pattern of primarily executive functioning deficits might be useful in distinguishing vascular dementia from Alzheimer's dementia[15]. Standardized measures of verbal memory, non-verbal memory and executive functioning were administered to a prospective sample of individuals who later went on to autopsy. Findings revealed that persons with Alzheimer's dementia showed memory scores approximately one standard deviation lower than executive functioning scores. These researchers found similar impairments, contrary to expectation, among individuals with vascular dementia in the areas of executive functioning, verbal memory and non-verbal memory[15]. However, when comparing only cognitively

impaired subjects, those with Alzheimer's dementia continued to show more significant memory impairment; persons with vascular dementia demonstrated more notable impairment on measures of executive functioning, and none of the subjects with vascular dementia showed more significant memory impairment[15].

Researchers have also studied individuals who have suffered stroke, but with cognitive impairment insufficient to meet criteria for vascular dementia. Compared to controls, individuals with cognitive impairment following stroke without dementia demonstrated significantly worse functioning in areas of attention and executive functioning. Patients who suffered stroke and met diagnostic criteria for dementia demonstrated significantly more difficulty in the areas of orientation and memory. The authors concluded that deficits in attentional and executive functioning were frequently found among individuals who had suffered stroke. However, stroke patients manifesting difficulties with memory, orientation and language were more likely to meet criteria for cognitive impairment without dementia or formal dementia[16].

Limited research has been carried out in the area of individuals with cognitive impairment insufficient to meet diagnostic criteria for dementia following stroke, and there are no formal diagnostic criteria for this condition[17]. In a prospective investigation, authors administered a comprehensive battery of neuropsychological tests to individuals 3, 12 and 24 months post-stroke. They also gave a questionnaire assessing symptoms of cognitive decline to proxies familiar with the subject's behavior[17]. The authors concluded that the risk of going on to develop dementia following stroke was significantly higher among those patients who showed cognitive impairment without dementia before experiencing a stroke[17]. Finally, they indicated that neuropsychological assessment appeared to be more accurate as a measure of long-term assessment following stroke, whereas historical interview and proxy rating played an important role in ascertaining the presence of cognitive impairment without dementia before stroke[17].

There remain conflicting findings regarding the association between stroke and later cognitive decline or dementia. The question exists whether patients who experience stroke without significant cognitive impairment or dementia are at higher risk for later cognitive decline or more severe cognitive decline. This question was studied by authors who followed stroke patients over a 5 year period[18]. They noted that patient performance on memory testing declined over time following stroke, whereas their performances on tests of abstract reasoning, visual spatial functioning and language ability remained stable during 5 years. The presence of stroke was associated with more rapid decline of memory, but there was no association between stroke and decline in abstract reasoning, visual spatial functioning or language ability. These associations were reported as being stronger among men[18].

Individuals suffering lacunar stroke are also vulnerable to cognitive dysfunction. Specifically, researchers have frequently found mild neuropsychological problems, typically in executive functioning, acutely following lacunar stroke (*Figure 3*). Generally, cognitive functioning was not grossly impaired during the acute phase of lacunar stroke, but cognitive impairment and dementia were noted to often develop over the long-term after such events[19]. Those patients manifesting an atypical lacunar syndrome demonstrated the most impaired cognitive functioning, particularly on measures of executive functioning[19].

The relationship between white matter hyperintensities, as seen on MRI, and neuropsychological dysfunction has also been investigated in individuals 3 months post-stroke[20]. Level of white matter hyperintensities predicted deficits in the areas of processing speed, executive functioning, memory and visual spatial ability. However, such relationships were not seen in short-term memory or verbal conceptualization[20]. Independent associations were found between white matter hyperintensities and lesions lining the lateral ventricles, and processing speed and executive functioning. General cortical atrophy was highly correlated with a variety of cognitive deficits, though overall infarct volume was less predictive of cognitive ability. Finally, the strongest effects were found for mental processing speed and executive functioning, domains postulated to play a significant role in secondary difficulties with memory and visual spatial functioning[20].

The effect of regional white matter hyperintensities on cognitive functioning has also been studied. MRI whole-brain axial fluid-attenuated inversion recovery, or FLAIR, images were acquired from patients over 75 years of age to investigate the effect of regional white matter hyperintensities on cognitive functioning among individuals with stroke[21]. Individuals who had suffered stroke demonstrated a greater amount of white matter hyperintensities in all areas studied as compared to controls. Significant associations included performances on attention and processing speed tests with volume of both total and frontal white matter hyperintensities, as well as between performance on memory testing and volume of temporal white matter hyperintensities[21]. However, no association was found between performance on measures of executive functioning and volume of frontal white matter hyperintensities, as might otherwise have been expected[21].

The role of the medial temporal lobe in memory functioning is well known. Medial temporal lobe atrophy among stroke survivors creates higher risks for memory dysfunction and the diagnosis of dementia. However, the role of medial temporal lobe atrophy in cognitive domains other than memory among individuals who have suffered stroke is less well understood. In an effort to address this area, authors studied a sample of individuals with MRI 3 months following stroke[22]. Those patients with moderate to severe medial temporal lobe atrophy demonstrated poor performances on measures of learning, story recall, visual reproduction, visual spatial reasoning and processing speed. However, participants demonstrating no, mild or moderate to severe atrophy did not differ in their

performances on measures of attention, cognitive flexibility, verbal fluency or conceptualization[22]. The authors concluded that, among older individuals with stroke, medial temporal lobe atrophy was well correlated with memory and visual spatial functioning, but unrelated to the areas of verbal and executive functioning[22].

There is some indication that memory difficulties following stroke may be reversible to varying degrees. Researchers have noted difficulties in memory functioning following stroke in up to 23–55% of patients after 3 months. However, after 1 year, these percentages declined to 11–31%[23]. Those patients manifesting larger stroke volume, white matter lesions and medial temporal lobe atrophy showed worse memory functioning, as would be expected. The authors concluded that the presence of deficit attenuation among individuals with stroke indicates the need for follow-up neuropsychological evaluation, after ~1 year, to assess for improvement in patient functioning toward more appropriate treatment[23].

Another group of researchers looked at the development of delayed dementia following stroke[24]. Using a comprehensive neuropsychological evaluation, these authors found that severity of expressive language difficulties was the only significant predictor at 3 months associated with dementia at a 15 month follow-up. They also noted that 50% of their sample manifested some spontaneous improvement in global cognitive functioning between the first evaluation and the follow-up testing at 15 months[24]. These authors concluded that delayed dementia is common among older patients with stroke. They noted, however, that the typical criteria for early cognitive impairment are not useful as predictors for the development of dementia in stroke patients and that most stroke patients show some improvement over time[24].

DIFFERENTIAL DIAGNOSIS

The clinician is frequently presented with the role of differential diagnosis in individuals with symptoms of dementia. Patients may have memory impairment with mood disorder and other cortical signs stemming from a variety of conditions. Once depression is ruled out as the primary cause for an individual's cognitive difficulties, the most frequent delineation, statistically speaking, will be between Alzheimer's dementia and vascular dementia. Other causes need to be considered and ruled out, but the vast majority of patients will have dementia from one of these two disorders.

Differential diagnosis is then made by evaluating the patient's presentation in the areas of onset, progression, focal neurological signs and symptoms, memory functioning, executive functioning, the presence of vascular risk factors and neuroimaging[2]. Individuals with Alzheimer's dementia typically manifest a gradual onset and a constant and insidious cognitive decline. Focal neurological signs or symptoms are usually absent, and their memory is typically impaired early and severely. However, individuals with Alzheimer's dementia do not typically show impairment on measures of executive functioning until later on in the course of the disease. Vascular risk factors are usually less common, though not necessarily, and neuroimaging is typically within normal limits with the exception of some possible hippocampal and perhaps parietal lobe atrophy[2].

In contrast, patients experiencing vascular dementia show either a sudden or a gradual decline with a slow and typically stepwise progression. Focal neurological signs and symptoms are often present. The patient's memory will be typically only mildly affected, often times with preserved encoding in the face of retrieval deficits. Executive functioning, however, usually manifests more severe impairment earlier in the course of the disease. Finally, patients with vascular dementia show obvious vascular risk factors, including strokes and transient ischemic attacks, and neuroimaging usually reveals infarcts and white matter lesions[2].

When considering neuroradiographic evidence from an individual with dementia, several factors are considered, including global cortical atrophy, medial temporal atrophy, white matter lesions and strategic infarcts. Alzheimer's dementia manifests typically with medial temporal atrophy, whereas vascular dementia usually shows more global atrophy. Temporal atrophy occurs in nearly 100% individuals with Alzheimer's dementia, as well as in many cases of vascular dementia. Strategic infarctions in vascular dementia involve areas crucial for normal cognitive brain functioning. These include the middle cerebral artery territory involving parieto-temporal or temporo-occipital association areas, the posterior cerebral artery territory including the paramedian thalamic region and the inferior medial temporal lobe (fusiform gyrus), watershed infarctions of the superior frontal and parietal lobes and lacunar infarctions of the bilateral thalami.

TREATMENT OF VASCULAR DEMENTIA

Individuals suffering from stroke do not enjoy many available treatments for associated cognitive difficulties. Given the variability associated with vascular dementia, the disorder does not lend itself to a specific treatment[1]. Whereas some spontaneous recovery of function is sometimes seen, and rehabilitation and accommodation can help improve an individual's functioning post-stroke, medical treatments for cognitive difficulties following stroke have been sparse. With a better

Table 2: Atrophic changes in Alzheimer's dementia and vascular dementia

Imaging finding	Alzheimer's dementia	Vascular dementia
Hippocampal atrophy	+++	++
Temporal atrophy	++	+
Frontal atrophy	−	+
Parietal atrophy	++	+
Lacunes	−	+++
WMLs	−	+++
Strategic infarcts	−	+++

WMLs: white matter lesions.

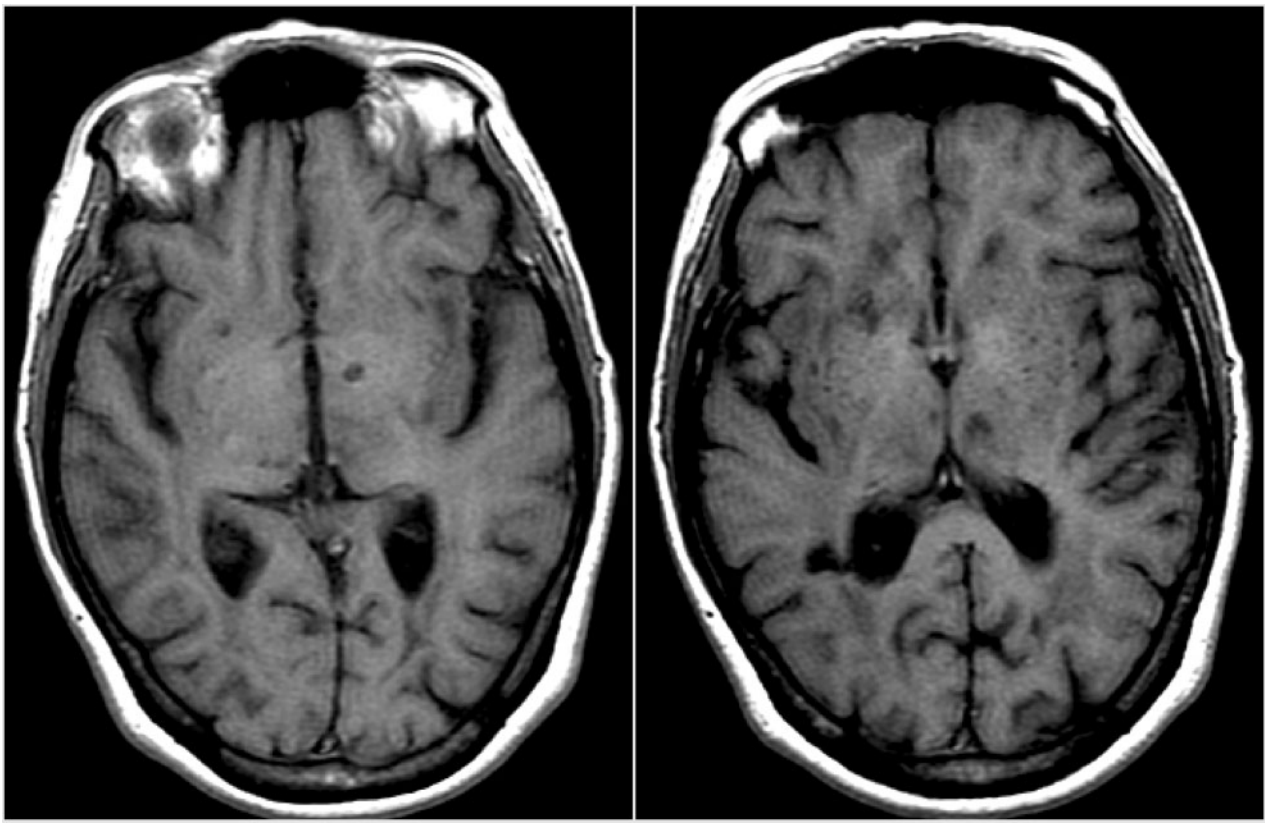

Figure 3: T1 weighted magnetic resonance image demonstrating multiple lacunar infarcts appearing as 'black holes'. Strategic infarcts involving both thalami are present

understanding for the role of acetylcholine in the areas of new learning and memory, cholinesterase inhibitors were developed and used in the treatment of memory impairment in individuals with Alzheimer's dementia[25]. Furthermore, N-methyl-D-aspartate (NMDA) receptor antagonists have also been recognized as effective in the treatment of cognitive impairment for some individuals with Alzheimer's dementia[25]. The question then naturally follows: Can these medications help improve cognitive functioning among individuals with other forms of dementia, specifically vascular dementia?

To this end, researchers have investigated the usefulness of these medications in the treatment of individuals with vascular dementia and vascular cognitive impairment[1,25]. A recent review of these studies indicated that donepezil was the best tolerated and most effective of available cholinesterase inhibitors. Galantamine also showed some effectiveness, but was less well tolerated[25]. There was insufficient evidence to recommend the use of rivastigmine in the treatment of individuals with vascular dementia according to some researchers[25], although others note its apparent beneficial effects among persons with Alzheimer's dementia with significant vascular risk factors[1]. Finally, the NMDA receptor antagonist memantine was well tolerated among persons with vascular dementia, but did not demonstrate a consistent cognitive benefit[25]. The authors noted that both cholinesterase inhibitors and NMDA receptor antagonists provided some potential benefit in the treatment of patients with vascular dementia and vascular cognitive impairment[25].

However, there is an increasing body of literature, which calls into question the efficacy of cholinesterase inhibitors in the treatment of dementia and the theory upon which it rests. Current research points to cerebrovascular pathology as a significant factor in the development of non-genetic Alzheimer's dementia[26], and several researchers are investigating the role of chronic brain hypoperfusion (CBH) as a risk factor for Alzheimer's dementia[27]. CBH has been found as a precipitant of mild cognitive impairment, and as the most effective predictor for the later development of Alzheimer's dementia[28]. In the compromised or older individual, CBH leads to progressive metabolic changes on a subcellular level within particular brain regions (hippocampal, parietal, etc.), which cause a neurodegenerative state and elicit dementia[28,29]. As such, there is mounting evidence that Alzheimer's dementia may best be managed as a vascular disorder with neurodegenerative effects[29].

Treatment of vascular dementia also includes prevention and attenuation of potential risk factors[2]. Whereas patients have little control over some risk factors, including gender, ethnicity and age, other risk factors, including hypertension and hyperlipidemia, can be modified[2]. Hypertension is an important risk factor with its significant role in the occurrence and recurrence of stroke. Successful treatment of hypertension signifi-

cantly reduces patient risk for recurrent vascular events[2]. Furthermore, lowering patient blood pressure appears to lessen the risk for the development of, and the severity of, dementia[1]. Reducing and controlling hyperlipidemia is also associated with reduced risk for stroke and associated dementia[2].

Investigational treatment methods for dementia are progressing and include omental transposition to the brain in patients with Alzheimer's dementia. The placing of omentum directly on the human brain has been shown to significantly increase cerebral blood flow[27]. In a series of ten patients with severe Alzheimer's dementia, omental transposition resulted in both objective and subjective improvement, particularly for patient functional status[27]. This is not entirely unexpected, as omental transposition has been found effective in the treatment of cerebral infarction and spinal cord transection as well[30]. The efficacy of this treatment appears at least partially due to the angiogenic and neurotrophic properties of omentum and its ability to help instigate revascularization of injured tissue[30].

CONCLUSION

Vascular dementia is a significant source of dependence and disability for patients. Although most stroke survivors go on to show some improvement over time, a large percentage eventually develop significant symptoms of dementia. Our comprehension for the manifestations of vascular dementia has shown notable recent improvement, and we are gaining a better understanding of its neuropsychological profile and how it differs from, and is similar to, other causes of dementia, most importantly, Alzheimer's dementia. This ability to recognize and identify the characteristic similarities and differences between Alzheimer's dementia and vascular dementia leads to improved treatment planning. Continuing research is providing answers regarding the appropriateness of newer treatments for vascular dementia and the benefit of modifying risk factors.

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