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Review Article

Vascular Dementia: Diagnosis and Management

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Abstract

Dementia is both increasing in prevalence and being better diagnosed with 10million new cases every year. The second most common is Vascular Dementia which will be the focus of this review. This also has global impact and there is real concern about what the future with a growing number of people facing this condition at some point over the course of their lifetime as they age. Vascular dementia is potentially preventable in many cases and increasing physician and public knowledge of the condition could make a real dent into reducing numbers and/or severity of this condition. Within this review the following topics are explored in more depth: the overlap with Alzheimer's Dementia, Imaging features, Risk Factors and Secondary prevention strategies. This narrative review aims to bring the reader up to date with current concepts in the pathophysiological processes, diagnosis and management of this condition.

Introduction

Dementia is increasing in numbers with 10 million new cases every year and accounts for 11.9% of years lived with disability [1]. This figure includes all types of dementia, for the purposes of this review the focus will be on vascular dementia which is the second most common form comprising approximately 20% of the cases when considered as a separate entity to Alzheimers Disease [2]. The two often overlap in an older population in which case this can be termed a mixed type dementia and with better imaging modalities there is an increasing awareness that vascular disease is strongly associated with Alzheimer's dementia [3,4]. It is more probable that the two pathologies co-exist in a majority of patients and combine to produce progressive decline in cognitive function. This adds another dimension of understanding to a vascular dementia other than being stroke associated cognitive decline. In an aging population with better awareness and access to diagnostic resources the numbers of dementia cases are shown to be large and growing1. Projected figures assume a reliable diagnosis rate across the population. This is not a safe assumption and is probably contributing to the underestimation of the impact of vascular disease to come. Large parts of the world still do not have access to good quality healthcare or diagnostics and prevailing concepts of aging include cognitive dysfunction as an inevitable part of the process rather than a sign of pathology. Vascular dementia can also present in a subtle way delaying diagnosis or simply not being recognised as a disease driven process. It seems this is the tip of the iceberg and we will probably see far more cases than predicted with significant burden on healthcare systems, social care and individuals worldwide.

Vascular dementia occurs a consequence of damage to the brain parenchyma caused by small vessel disease, microinfarcts, haemorrhage and ischaemic stroke [5,6]. Disease accrues over time and may begin in either a subtle way with gradual decline or with a larger more dramatic event such as stroke with then step wise decline as strokes recur. Managing modifiable vascular risk factors such as hypertension, obesity, smoking, diabetes mellitus can reduce or slow accumulation of cerebrovascular disease and resulting cognitive decline [7,8].

Rehabilitation in those with memory problems remains a challenge for therapists and physicians. 'Is there carry over?' is a frequently asked question when starting a rehabilitation programme, the questioner wishing to establish if the patient can recall elements of practice from the session prior. Another common question is about motivation to engage with the process and if there is insight into impairments. The current approaches to rehabilitation in

dementia patients are of cognitive stimulation, training or rehabilitation all being distinct but can be used as a multimodal intervention. A Cochrane review [9] of 11 trials of cognitive rehabilitation in both vascular dementia and Alzheimers patients showed that cognitive training/rehabilitation did not seem to have significant positive effect. There was admittedly limited evidence from small scale studies and only one randomised controlled trial. This was over ten years ago and little seems to have changed over that period of time with more recent European Guidelines confirming the same [10]. The purpose of the review is to clarify current approaches to cognitive stimulation, training and rehabilitation and discuss advances in the field with future directions.

Diagnosis

This is usually based on a presentation of stroke or multiple strokes with a recognition of accompanying cognitive impairment with a radiological correlate. Clinical and imaging diagnostic criteria setting has not been very successful over the years the criticism being that they miss cases or cannot differentiate well between mixed and predominantly vascular cases [11,12]. One point of weakness is that they do not weight small vessel disease sufficiently, this is increasingly being recognised as a cause of vascular dementia in addition to the traditional 'multi infarct dementia' concept. Newer DSM criteria and AHA/ASA seem to be more able to discriminate mixed dementia from probable vascular dementia and therefore can be useful in clinical practice to aid treatment planning and conversations with patients about prognosis [13]. Imaging is key in accurate diagnosis and usually requires access to MRI scanning. Access to MRI scanning in low and middle income countries is an issue with the distance to travel, cost and accessibility being prohibitive for more than 60% of the world's population [14]. This means that for the majority the diagnosis will be made on clinical history alone. Typically the natural history of the disease is one of a 'step like' progression with sudden onset drops in level of cognitive ability linked to stroke episodes which are separated from each other in time. This taken in conjunction with a past medical history of vascular risk factors and family history can be sufficient if there is no access to imaging. MRI Imaging is reviewed for the presence of small vessel disease, territorial infarcts, lacunes, enlarged Virchow Robin spaces and microbleeds [15]. MR angiogram of extra and intra cranial vessels can show stenosis or blockage due to atherosclerosis which can result in infarct or chronic hypoperfusion and microinfarcts in the supplied brain parenchyma.

The most commonly used cognitive assessments in clinical practice are still Mini Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MOCA). They are often used in initial tests in patients with any type of cognitive impairment and serial testing can be used to track progress over time. They are both versatile in that they can be delivered at the bed side, are quick enough to be completed in one clinic appointment and can be completed by any trained healthcare professional. One meta analysis [16] found that the MMSE had a summaried 0.62 sensitivity and 0.87 specificity vs MOCA 0.89 sensitivity and 0.75 specificity in those with mild cognitive impairment. The high sensitivity of the MOCA makes it useful in practice to be used for screening in those with concerns or symptoms of dementia with progression to more nuanced tests eg Addenbrookes Cognitive Examination, neuropsychological battery to be used after this. Differentiating affected cognitive domains does not add diagnostic value.

Lesion Location as linked to Specific Impairments

As the pathology associated with vascular dementia can occur anywhere in the brain the resulting cognitive impairment will be heterogenous as will the linked functional impairment. Higher volume infarcts produce deficits in line with recognisable patterns which produce predictable impairments dependent on vascular territory affected eg apraxia, dyscalculia. Support vector regression-based lesion symptom mapping has been used to locate strategic areas of the brain which produce cognitive deficit when infarcted [17]. Simultaneous Montreal Cognitive Assessments allowed for affected domains to be linked to infarct location. Lesions in the left hemisphere were more associated with language and memory dysfunction than those on the right. In addition global post stroke cognitive impairment was more probable when 15 sites were affected key ones being : basal ganglia, internal capsule, thalamus, corpus callosum, angular gyrus, cingulate cortex and frontal subcortical areas. This is helpful when predicting which patients will have significant post stroke cognitive impairment. Being able to pass this information on to patients and carers allows them to prepare for the transition into their post stroke life and for the future.

Cortical cerebral microinfarcts are probably more common than previously thought with association with white matter hyperintensity and atrial fibrillation. They are not seen on conventional MRI imaging and despite a mean diameter of 0.2mm the peri infarct gliosis and remote effects of infarction make their impact larger than their size [18,19]. This adds to the understanding of the pathology and progression of vascular dementia as a process as opposed to the original concept of multiple territory infarcts leading to patients accumulating cognitive deficits.

Risk factors and Associations

Making a diagnosis and managing a patient with cognitive impairment involves an evaluation of their vascular risk. Risk factors for vascular dementia are either modifiable or non modifiable and overlap with those for cardiovascular disease. Modifiable risk factors are diabetes mellitus, obesity, hypertension, hyperlipidaemia, smoking, atrial fibrillation. The biggest non modifiable factor is age [20,21] and the incidence of risk factors such as hypertension , diabetes and atrial fibrillation also all increase with age. Disease in one vascular bed predicts disease elsewhere and there may be accompanying cardiac disease, peripheral vascular disease or aortic atheroma. Risk factors are not additive but rather multiply when in combination and produce escalating risk. Hypertension is the leading risk factor in influencing risk of vascular disease, when managed in mid life onward there is a significant reduction in stroke risk [21,22]. The WHO has produced a global report detailing the huge increase in hypertension in both Europe and Americas, South Asia and Western Pacific areas. Just over half of cases have been diagnosed, under half are treated and only 21% are sufficiently con-

trolled to reduce risk [23]. The numbers are huge and will certainly have impact on the number of cases of vascular dementia over the coming decades even if public health initiatives work in improving access to measuring and monitoring. Access to medications remains an issue in developing countries, even if anti hypertensives can be bought over the counter there is often no access to monitoring of efficacy and also side effects.

Stroke risk factors and the cognitive function were examined in the Framingham Offspring Study [24] and found a significant association between stroke vascular risk factors and poorer cognitive functioning. A 10% increase in 10-year stroke risk had significant impact on the following tasks: abstract reasoning, visual-spatial memory, visual organization, concentration, visual scanning, and tracking. This was in a patient cohort with no known diagnosis of stroke or dementia. This makes the role of primary physician vital in identification and control of vascular risk factors. It also means that a patient who reports of mild neurocognitive dysfunction should have prompt evaluation of risk and not have these be labelled as a symptom of aging.

There are multiple other factors being investigated which may or may not influence risk of developing vascular dementia these include composition of the gut microbiome, climate change and air pollution [22]. The gut brain axis is being explored as a possible influence on cognitive function and patients with dementia do show altered gut microbiome composition [25]. The complexity of the relationship is not understood but there is some evidence emerging that probiotics may be helpful for patients with mild cognitive impairment. There has been some interest in whether statin use worsens cognitive function which leaked into the media within the last ten years and led some patients feeling discouraged about regular statin use. Meta analyses have found no significant effect of statin use on cognitive function [26].

Antiplatelets

The use of anti-platelets in an older population is not without risk and the benefit can sometimes be difficult to quantify. Without large scale trials or observational studies looking at the use of anti and dual antiplatelet regimes it can be hard to know if there will be significant slowing of disease progression in the case of small vessel disease or stroke prevention without causing harm. Two helpful trials from which we can extrapolate information were the OXVASC study data [27] looking at bleeding risk in older patients and also the CHANCE II trial [28]. The CHANCE II subgroup analysis of 406 over 80s found using clopidogrel and aspirin was not inferior in recurrent stroke prevention to aspirin and ticregalor. This is somewhat of a relief as there is a reported higher risk of intracerebral haemorrhage when using ticregalr at any age. There were significant differences of severe or moderate bleeding with a hazard ratio of 8.4 in the over 80s vs the younger age groups and an overall higher mortality. All the patients in CHANCE II [28] did have the CYP2C19 LOF alleles which are present in 30% of whites and 60% of Asians (this was a China based study) which reduces our ability to extrapolate to the population. An OXVASC cohort of over 75s on anti-platelets (the majority would have been on single drug regime at this time) showed a significant number of bleeds with at least 50% being from the upper gastrointestinal tract. There was significant reduction with PPI use. Overall, by 85 years of age the annual major bleed rate was 4.1%. Judging risk has always been difficult with BAFTA trial [29] some years ago finding the relative risk of an extracranial bleed was marginally lower on warfarin vs. aspirin. This leaves us in a position of knowing that aspirin is not to be trifled with in the older age groups and that using a proton pump inhibitor concomitantly is probably a good idea. Proton pump inhibitors come with their own problems: increased risk of chest infection, low magnesium, loose stool to name a few. Guidelines have not been adjusted for the older age group due to paucity of data and there is a growing need for more high-quality studies in the older age groups to help us judge better the risk these drugs provide and at which point futility creeps in.

Conclusions

Concepts of Vascular Dementia have evolved over the years and there is now a better understanding of what the pathology is, what it looks like on imaging and what influences disease progression. Identification of small vessel disease as a cause of dementia was a key point in developing our understanding of this as a spectrum of arterial disease processes. There are still many aspects to be explored further with the pressure on as the global burden rapidly increases.

Acknowledgement

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Conflict of Interest

None.

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