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RESEARCH ARTICLE

ARTICULATION OF ALZHEIMER'S DISEASE WITH PERIODONTAL DISEASES

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ABSTRACT

Alzheimer's disease is the unrivalled cause and commonest form of dementia. The exact etiology and pathophysiologic mechanism of Alzheimer's disease is still not fully understood. However it is hypothesized that, neuro inflammation plays a critical role in the pathogenesis of Alzheimer's disease. Subjects, particularly in the geriatric category should be strongly motivated and frequent visits for periodontal maintenance should be duly emphasized. The dental professional and neurologist need to co-ordinate consistently regarding the methodical management of geriatric patients.

INTRODUCTION

Alzheimer's disease is the unrivalled cause and commonest form of dementia. The exact etiology and pathophysiologic mechanism of Alzheimer's disease is still not fully understood. However it is hypothesized that, neuroinflammation plays a critical role in the pathogenesis of Alzheimer's disease. Vitamin A, C and E have antioxidant activity, which have been investigated for its prevention from neuronal death and improving neuronal function through maintaining mitochondrial homeostasis.[1] Vitamin E may modulate signal transduction pathways and participate in the synthesis pathways of neurotransmitters. Several epidemiological studies have indicated a relationship between blood concentrations of antioxidant micronutrients and cognitive impairment. Periodontitis is known to elicit a "low grade systemic inflammation" by release of pro-inflammatory cytokines into systemic circulation.[2] This review demystifies the possible role of periodontitis in exacerbating Alzheimer's disease. Periodontitis may bear the potential to affect the onset and progression of Alzheimer's disease. Periodontitis shares the two important features of Alzheimer's disease namely oxidative damage and inflammation, which are exhibited in the brain pathology of Alzheimer's disease. Periodontitis can be treated and hence it is a modifiable risk factor for Alzheimer's disease.[3]

SCAVENGING THE FREE RADICALS

Brain tissue is particularly vulnerable to free-radical damage because of its low level of endogenous antioxidants (Reiter, 1995). Neuropathological studies documented typical lesions from exposure to free radicals in the brains of patients with Alzheimer's disease (Behl, 1997; Christen, 2000; Pratico & Delanty, 2000; Varadarajan et al., 2000). Several studies suggest that 'oxidative stress' may play a role in the changes in the brain that cause Alzheimer's disease.[4] Oxidative stress can lead to 'attack' on brain cells by chemicals called free radicals. It is these free radicals that cause oxidative damage. Free radicals are produced by cells as a by-product of energy production, and therefore are a result of normal functioning.[5]

Many studies have provided evidence for the deleterious consequences of oxidative stress products on certain cellular targets in AD. Protein oxidation and the oxidation of nuclear and mitochondrial DNA have been observed in both AD patients and in elderly patients without AD, but the oxidation of nuclear and mitochondrial DNA appears to be present in the parietal cortex , whereas protein oxidation appears to be more marked in AD patients in the

regions presenting the most severe histopathologic alterations . In addition, increased lipid peroxidation in the temporal lobe where histopathologic alterations are very noticeable in the AD brains has been observed. The APOE genotype and those with the ε4 allele seem to be more susceptible to peroxidation than those without this allele.[6]

They have both harmful and beneficial effects in cells. Free radicals alter the structure and function of substances in the body. For example, in high concentrations they can damage proteins and DNA. They can damage cell membranes (the protective covering of cells), cause tissue damage and inflammation, and generally disrupt chemical processes within the body. To prevent this disruption and damage, our bodies naturally make, and acquire from food, molecules that react with free-radicals. These are generally called 'antioxidants'.[7] Huge numbers of different substances can act as antioxidants. Some of the most well known include vitamin C, vitamin E, beta-carotene and other related carotenoids, flavonoids, phenols, and many more. Putting all these chemicals into one large group is actually quite misleading. Each antioxidant has a different chemical composition, behaves slightly differently, and has a slightly different role. This makes it difficult to examine 'antioxidants' as a general and single aspect in dementia risk. [8]

UNMASKING THE RELATION

There is substantial evidence that brain (A^2) deposits become a nidus for innate inflammatory responses particularly in the context of microglial reactions to(A^2).microglia are small glial cells of mesodermal origin that are distributed throughout the gray and white matter of the nervous system. For these reasons activated microglia are widely considered to play a pivotal role in AD inflammation. chronic inflammation within peripheral organs might play a role in the exacerbation of the molecular pathogenesis of AD. One such inflammatory condition is periodontal disease. The inflammatory response that occurs in periodontal disease has been known to involve the development of various diseases, such as arteriosclerotic disease, DM, and obesity, and the incidence of premature and low birth weight infants .[9] In addition, periodontal disease has been reported to involve cerebral abscess formation. Periodontal disease-related bacteria are spread systemically through the blood vessels and respiratory tract, suggesting its possible direct effect on the target organs. In addition, inflammatory mediators such as cytokines, which are produced in the

local periodontal tissue, are carried hematogenously to the target organ and thought to worsen the inflammatory response.[10]

The flora of periodontal disease consists largely of gram negative bacteria. Current research has identified brain receptors specific for gram negative bacteria. Brain infections by gram negative bacteria have been linked to alzheimer's etiology, specifically late-onset sporadic AD. Periodontal pathogens in periodontitis like Aa, Pg, Pi, Tf, Fn are tissue invasive. This property enables the pathogens to escape from the extracellular host defense system and replicate in the host tissues. The spirochetal species in the periodontal plaque possess a wide range of virulence factors aiding in confronting with the host defense mechanisms and enhancing its ability to invade the periodontal host tissues. Spirochete plaques or masses in the brain resemble senile plaques of AD.[11] Gene polymorphism involved in periodontal inflammation could be a conceivable nexus between periodontitis and AD. It is proposed that inflammation may act as an elusive link between periodontitis and pathogenesis of AD. Till date there is no evidence of a causal relationship between periodontitis and AD. Periodontitis can intensify the systemic bioburden and contribute to a "low grade systemic inflammation". It may be accounted as one of the possible risk factors for perpetuating the neurodegenerative process in AD. [12]

Bretz and colleagues found significantly higher levels of IL-6 in the blood of those with extensive periodontal disease compared with controls. This findings is noteworthy because IL-6 is associated with local production of amyloid protiens, and in alzheimer's brain it may regulate production of amyloid protiens found in neutritic plaques, cytokines have been implicated in pathophysiology of several psychiatric disorders, including AD because of their ability to stimulate neurochemical, neuroendocrine and neuroimmune changes in the brain.As noted, inflammatory mediators can damage synapse and neurons and activate microglia and inflammatory cascade.IL-1 is particularly relevant to pathology of AD. Since it is over expressed in neuritic plaques.13 The cell wall of gram negative bacteria contains lipipolysaccharide (LPS) that induces a number of host defenses. Lipopolysacchride stimulate certain inflammatory cytokines that are associated with microglial activation and altered processing of amyloid precursor protein.

CONCLUSION

It is proposed that bacterial and viral infections commonly found in periodontal disease may impact the brain, either directly or via systemic signals to the brain and contribute to alzheimer's disease. In this modern aging society, preventing periodontal disease and maintaining oral cavity function will become increasingly more important. Subjects, particularly in the geriatric category should be strongly motivated and frequent visits for periodontal maintenance should be duly emphasized. The dental professional and neurologist need to co-ordinate consistently regarding the methodical management of geriatric patients.

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