BIOSCIENCES BIOTECHNOLOGY RESEARCH ASIA, April 2014. Vol. **11**(1), 259-261

Alziemer's Disease and Periodontal Disease Bidirectional Interrelationships

V. Ramya*, Bhuvaneshwarri, Preethe Paddmanabhan and N. Manisundar

Department of Periodontics, Sree Balaji Dental College and Hospital,
Bharath University, Chennai, India.

dx.doi.org/10.13005/bbra/1264

(Received: 10 January 2014; accepted: 05 February 2014)

Alzheimer's disease is the most common form of dementia. It is a brain disorder which gradually destroys the ability to reason, remember imagine and learn. Over the course of the disease people with alziemer disease no longer recognizes themselves or much about the world around them. Periodontal infections may result in harmful pathogenic products leading to systemic inflammatory responses. Elevated systemic inflammatory response may contribute to the exacerbation of existing brain pathologies. Infections may also contribute to vascular pathology with the potential to impact brain function.

Key words: AD- alziemer'sdisease, CDR –clinical dementia rating.

Approximately 1% of the population between 65 and 69 years of age has been diagnosed with AD and the incidence increases logarithmically with age, with 5% of individuals at 75 years of age, and 22%at age 85.the clinical course of AD from the first identifiable symptoms averages 8-10 years but may continue as long as 20 years .a clinical diagnosis of AD is based on cognitive assessment tools including the MINI MENTAL STATE EXAMINATION(MMSE) and clinical dementia rating scale (CDR).A cognitively normal elderly individual can have MMSE score of 26-30 while an individual with mild AD usually has a score Â23.The expected decline in individuals with AD is about 3 points per year. A CDR score of 1.0 or higher is an indication of AD.[1]

* To whom all correspondence should be addressed.
Mob.: +91-9894383459;
E-mail: dr.ramya@yahoo.co.in

The major pathological hallmarks of AD, first described by Alios alziemer in 1907, the classic pathologic hallmarks of AD are two types of aggregate

The β-amyloid plaque the main constituent of which is the 40-43 aminoacid, Long amyloid beta(A^2) peptide, The neurofibrillary tangle,the main constituent of which is a structural protein.

In addition amore recently accepted hallmark of AD is brain inflammation, specifically an innate inflammatory response by the nervous system that is likely to reflect an attempt to clear (A^2) deposits and other forms of AD pathology[1]

Pathogenesis of alziemers disease

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.[2] At rest, they are believed to play supportive roles for neurons. However fundamentally they are specialized immune cells, related to macrophages, which can take on attack and pathogenic roles when activated. Like activated microglia secrete a wide range of inflammatory mediators, are capable of

migrating to sites of inflammatory activity and exibit scavenger responses to damaged tissue and accumulations of abnormal proteins. By contrast there seems to be little to no involvement of leukocytes or monocytes. For these reasons activated microglia are widely considered to play a pivotal role in AD inflammation.

Relationship between periodontal disease and alziemer'sdisease

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 alziemers etiology, specifically late-onset sporadic AD. A recent histologic study demonstrated the presence sof gram negative bacteria Chlamydia pneumonia in cells of affected brain regions in 17 of 19 post mortem alziemer's brains, while brains of controls were not infected in individuals with oral hygiene the number of oral pathologic bacteria reaching circulation is low.[3]

It is also possible that pathogenic bacteria do not infect the brain but rather induce a systemic inflammatory response leading to injury of brain tissue. Since host responses to periodontal disease, such as up regulation of proinflammatory mediators, show significant positive correlation with coronary artery disease and premature birth, neuropathological responses may also be induced ever, this number increases twofold to tenfold in persons with periodontal disease.[4]

Inflammatory mediators of periodontal disease

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 amyloidprotiens, and in alziemers 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.[4] 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 overexpressed in neuritic plaques. In addition, IL-1 increases synthesis of beta-amyloid precursor protein and activates astroctyes suggest that long term systemic exposure to periodontal pathogens and subsequent chronic production of inflammatory

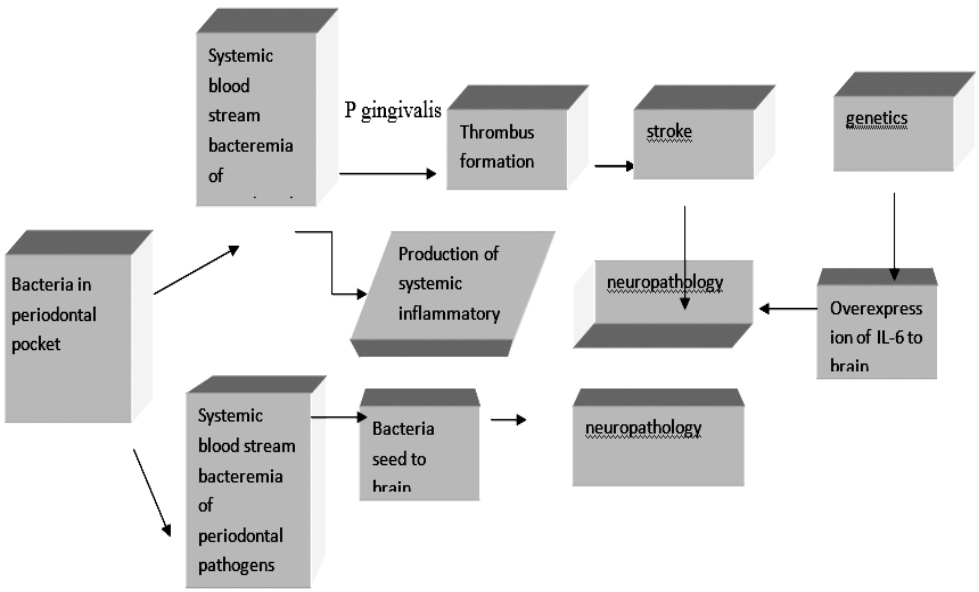

Fig. 1. Flowchart model of biologically plausible mechnasim underlying a potential association between periodontitis and neuropathy

mediators may precipitate neuropathological changes[7].

The third national health and nutrition examination survey (NHANESIII) showed that gingival bleeding, loss of periodontal attachment and Serum P.gingivalis IgG were significantly associated with cognitive function even after extensive adjustments for confounders[8].

Pathogenic products

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[5].

Mechanism involved in spirochete-host interaction and their similarities to alziemer'sdisease

The strong neutrophism of spirochetes is well known.spirochetes can invade the brain and generate latent, persistent infection in addition hematogenous to dissemination ,they can spread via lymphatics ,and along nerve fiber tracts accordingly periodontal invasive spirochetes were detected along the trigeminal nerve and in trigeminal ganglia.[5] They might also propagate along the fila olfactoria and tractus olfactorius which would be in harmony with olfactory hypothesis and with previous observations showing that the olfactory tract and bulb are affected in the early stages of the degenerative process in AD. [5]Spirochetes attach to host cells through their surface components including collagen binding proteins, bacterial amyloids and pore forming proteins through activation of plasminogen and factor XII,bacterial amyloids contribute to inflammation and modulate blood coagulation .The innate immune system enables host cells to recognize spirochetes, execute proinflammatory defenses, and start adaptive immune responses.[6]

CONCLUSION

It is proposed that bacterial land viral infections commonly found in periodontal disease may impact the brain, either directly or via systemic signals to the brain and contribute to alziemer's disease. If systemic infection and inflammation have been proved longitudinal studies to be the contributors of alziemer's disease several preventive measures and treatment strategies would be implied.

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