Review Article

PHATHOPHYSIOLOGY OF ALZHEIMER'S DISEASE

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ABSTRACT:
Alzheimer's disease is the age related degenerative disease of the nervous system. Initially, episodic memory decline is followed by loss of short term memory. This disease is due to premature aging of the brain. Its prevalence is higher in females. Patients are not able to perform daily activities and they require constant care. Old people who remain involved in intellectual activities and exercise have a decreased risk for this disease. Intake of high fat and carbohydrate rich diet increases the risk.
It is concluded that Alzeimer's disease is the most important neurodegenerative disease due to premature aging of the brain menifested by loss of memory and impairment of cognitive and other brain functions. Intellectual activities and physical exercise reduce risk for this disease.

Key Words: Dementia, Memory, Premature aging

INTRODUCTION

Alzheimer's disease (AD) is the most important age related disease due to degeneration of parts of the brain. Impairment of short term and episodic memory initially occurs with inability to recall recent events. It is followed by decline of cognitive and intellectual brain function.[1–3] There is progressive degeneration due to premature aging of the brain. Patients are unable to perform routine daily activities and need continuous care.[4] It has been named after the German Psychiatrist and pathologist, Alio Alzheimer in 1906. (Fig – 1).[5] It is a common type of dementia in old people. In western countries, it is a highly costly disease. Incidence of this disease doubles with every 5 years of the age. At the age of 60 years, it is 1% and at the age of 85 years, it is 30%. Prevalence of the disease is higher in females because of their longer life span. In two third of patients of dementia, Alzheimer's disease is the cause.[4-7]

Due to progressive brain deterioration, patients cannot live independently. Speech becomes difficult due to their inability to recall vocabulary resulting into incorrect substitution of words (paraphasias).[8]

Due to decreased motor coordination, falling can occur. As the long term memory declines, they fail to recognize their close relatives. Behavioral changes begin such as wandering, irritability, crying, aggression or resistance to care giving. Some patients show sun downing. Urinary incontinence can start. These changes pose problems for the close relatives and caregivers. These patients can be moved from home care to special care centers. In late stages of the disease, their mobility decreases to the point where they become bed ridden and unable to feed. The disease itself is not the cause of death. Infection of pressure ulcers or pneumonia can lead to death.[8-10]

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INHERITANCE

Autosomal–dominant inheritance is not common in cases of AD. Inheritance of the E4 allele of apolipoprotein E (APOE) gene is the known genetic risk factors.[11,12] 40–80% of patients with AD have at least one APOE 4 allele that increases the risk of the disease by 3 times in heterozygote and by 15 times in homozygotes.[13]

HISTOPATHOLOGY

The Histopathological feature in AD is loss of neurons and synapses in cerebral cortex and other parts of the brain leading to atrophy of temporal and parietal lobes, parts of the frontal cortex, hippocampus and cingulate gyrus.[14] There is degeneration of cell bodies of cholinergic neurons in these areas leading to deficiency of acetyl choline. Neuronal death and loss of synaptic transmission results into dementia.[15] Reduction in size of these parts of the brain can be seen by Magnetic Resonance Imaging (MRI) and Positron Emission Tomogrephy (PET).[16,17] Microscopy of these brain parts slow beta amyloid plaques. These plaques are dense insoluble deposits of beta amyloid peptide and cellular material around neuron.[18] Neurofibrillatory tangles are aggregates of microtubule associated protein tau that has become hyperphosphorylates.[19] It is rare to have levy bodies in the brain of these patients.[20] Size of beta amyloid plaques varies from 10 um to several hundred um.[7]

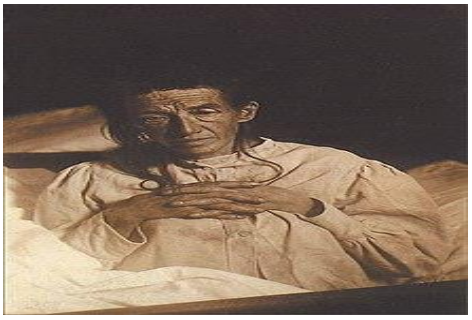

Figure I. Alois Alzheimer's patient Auguste Deter in 1902. Hers was the first described case of Alzheimer's disease.

DIAGNOSIS

Patient's medical history, history from relatives, observation of behavior, presence of specific neuropsychological features and absence of alternate conditions help to diagnose Alzheimer's disease.[21,22] Computed tomography (CT) or magnetic resonance imaging (MRI) or positron emission tomography (PET) can be used to exclude other subtypes of dementia.[23] In addition, it may predict conversion of mild cognitive decline to Alzheimer's disease.[24] Memory testing can determine the state of the disease.[25] Accurate diagnosis can be confirmed by postmortem examination of the brain.[26]

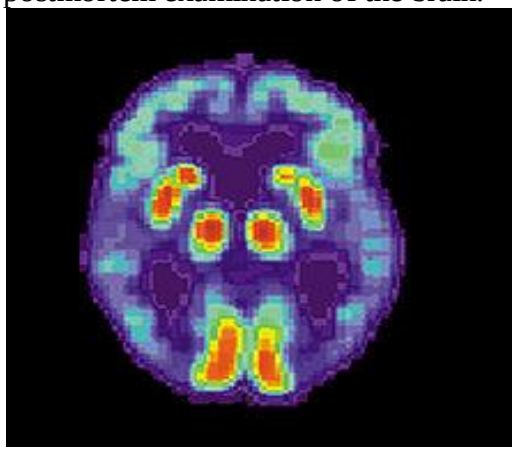

Figure II. PET scan of the brain of a patient with AD showing loss of function in the temporal lobe**.**

RISK FACTORS

Risk Factors Include

- Age
- Chromosome 14 (Presenilin 1 mutations)
- Chromosome 1 (Presenilin 2 mutations)
- Gene for amyloid precursor protein
- Mutation of chromosome 21
- Chromosome 19 Apo E allele
- Trisomy 2

- Mutation in Alpha –2 macroglobulin gene (late onset disease)
- Apolipoprotine E gene abnormality.

Cigarette smoking and intense intellectual activity can prevent the disease to some extent.[27]

Lifestyle factors like diet, exercise, social engagement and mental stimulation may determine the chances to develop Alzheimer's disease.[28]

Hormonal disturbances. Cortisol increases chances to develop this disease while estrogens decrease the risk.[7]

Cardiovascular risk factors, such as hypercholesterolemia, hypertension and diabetes are associated with a higher risk of onset and course of AD.[29,30] Statins have not been effective in preventing or improving the course of the disease.[31-33]

Non-Steroidal anti-inflammatory drugs (NSAIDs) decrease risk of developing AD.[34] NSAIDs can decrease inflammation related to amyloid plaques.[34] These do not appear to be useful as a treatment.[35] Long acting anti-cholinesterases that cross the blood brain barrier may improve cognitive function in these patients.[36]

People who engage in intellectual activities such as reading, playing board games, completing crossword puzzles, playing musical instruments, or regular interaction with other people decreases risk for Alzheimer's disease.[37] Education and learning a second language delays onset of this disease.[38,39]

Physical exercise decreases rate of dementia[38,40] and also reduces symptom severity in Alzheimer's disease.[41]

EFFECT OF DIET

In individuals on Japanese or Mediterranean diet, there is lower risk of AD.[42,43] Saturated fat and simple carbohydrate rich diet has a higher risk.[44] Cocoa, red mine and tea decrease the risk for AD.[45-47] Vitamins A,C,D folic acid, vitamin B_{12}, have no beneficial effect.[48-52] Selenium, zinc and omega – 3 do not benefit patient with Alzheimer's disease.[53-55]

CONCLUSION

Alzheimer's disease is the most common neurodegenerative disorder due to premature aging of brain characterized by dementia and impairment of cognitive and other brain functions. Intellectual activities and physical exercise reduce risk for Alzheimer's disease.

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