Review Article

Alzhiemer Disease: A Brief Review

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ABSTRACT

There is a spectrum of Alzheimer's disease, from early changes in memory to functional dependence and death. Using a case illustration, we review the assessment and diagnosis of mild cognitive impairment and the diagnosis and management of Alzheimer's disease at each stage, including the management of the disease's cognitive and behavioral / psychiatric aspects and end-stage and end-of-life care.

Keywords: Alzheimer's disease; dementia; Cholinesterase and neurodegenerative.

INTRODUCTION

The population of the world is aging rapidly, and by 2030 the number of people with dementia is expected to increase from 35 million today to 65 million. Living with Alzheimer's disease (AD), the most common cause of dementia, is 5 million or 1 in 9 people over the age of 65 in the United States. Alzheimer's disease is a progressive neurodegenerative condition linked to age with an immense unmet medical need. It is the most common form of dementia affecting approximately 5% of adults over 65 years. Approximately 10% of the adults older than 65 years, and 50% of the adults older than 90 years have dementia Cholinesterase inhibitor therapy in Alzheimer disease (AD) may provide cognitive and behavioral symptomatic improvement for some patients. Not all patients respond to cholinergic therapy; there is a response distribution from marked to no improvement.

Memory is one of the most complex functions of the brain and ultimately involves multiple neuronal pathways and neurotransmitters. Memory deficiency is an organic brain condition described as loss of intellectual ability of sufficient severity to interfere with work, normal social activities or relationships. of a person in the absence of gross clouding of consciousness or motor involvement[1].

ALZHEIMER'S DISEASE

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive impairment of episodic memory and other cognitive domains resulting in dementia and, ultimately, death. Alzheimer's disease (AD)is associated with loss of neurons in distinct brain areas[2]. Age, stress, emotions are conditions that may lead to memory loss, amnesia, anxiety, high blood pressure, dementia, or to more ominous threats like Schizophrenia and AD. Quality of life of senior citizens is adversely affected by dementia caused due to degeneration of the cerebral neurons[3]. Progressive memory and language impairment, disorientation, behavioral symptoms (hallucinations, delusions, paranoia), and psycho social impairment.

Dementia

Dementia is a psychiatric disorder (a collection of cooccurring signs and symptoms) involving a progressive loss of mental function. Dementia may affect different cognitive abilities, including memory, speech, thinking, decision making, visuospatial capacity, awareness, and orientation. Cognitive impairments are often associated with changes in personality, emotional regulation, and social behaviors in individuals with dementia.[4] Importantly, the cognitive and behavioral changes that occur with dementia interfere with employment, social activities, and relationships and affect the capacity of an individual to conduct daily routine tasks (e.g. driving, shopping, housekeeping, eating, managinal activity).

AD is the most common cause of permanent dementia in the United States, responsible for up to 70% of all cases of dementia.[5] Other forms of primary dementia include vascular dementia (1020%), Parkinson-associated dementia, Lewy-associated dementia, and frontotemporal dementia.

Epidemiology of AD

AD is a multifactorial disease with no known single cause, and its development and progression is associated with several modifiable and non-modifiable risk factors. Age is the major risk factor in the development of AD The risk of having AD increases exponentially with age, around doubling every 5 years after age 65. The vast majority of people with AD are 65 years of age or older and have 'late-onset' or 'sporadic' AD (95% of all cases). The development of AD before age 65, known as 'earlyonset' or 'family' AD (B5 percent of all cases), is associated with rare genetic mutations.

Moreover, people with Down's syndrome (trisomy 21) are at increased risk of developing early-onset AD. Sporadic AD

genetics are more complex and less well known. It is known that the apolipoprotein E (APOE) gene epsilon four allele located on chromosome 19 is a risk factor for sporadic AD development.[6] The prevalence of AD among females is higher, reflecting women's longer life expectancy. Lower educational achievement was associated with increased risk of AD.

Neuropathology of AD

AD is a progressive neurodegenerative brain disease which causes a major disturbance of normal brain structure and function. At the cellular level, AD is characterized by a progressive loss of cortical neurons, particularly pyramidal cells, which mediate higher cognitive functions.[7] There is also substantial evidence that AD cause synaptic dysfunction early in the disease process, disrupting the disease.

The medial temporal lobe, primarily in the entorhinal cortex and hippocampus, AD-related degeneration begins. Damage to these brain structures results in memory and learning difficulties that are commonly associated with early clinical manifestations of AD.

The degeneration then spreads throughout the cortex and parietal areas of the temporal association. As the disease progresses, degeneration can be seen in the frontal cortex and gradually in most of the remaining neocortex. The fact that AD causes damage to several limbic system component Hippocampal formation and the major fiber tracts connecting it to the cerebral cortex (fornix and cingulum), amygdala, cingulate gyrus, and thalamus are included This common pattern of neurodegeneration, affecting both limbic and neocortical regions, is strongly associated with the spectrum of cognitive deficiencies and behavioral changes that patients with AD experience. In addition to cognitive dysfunction in several domains (memory, language, reasoning, executive and visuospatial function), patients with AD have a diminished capacity to perform daily activities.[8] Patients with AD have an impaired ability to perform daily living tasks in multiple domains (memory, speech, thinking, cognitive, and visuospatial function) and often experience psychological, mental, and personality disorders.[9]

Diagnosis

Diagnosis Criteria: Alzheimer's disease clinical diagnosis follows a logical sequence as seen in many diseases: information from an information should be included in the history. Patient-related person; mental state assessment should include validated cognitive function testing; and physical examination should focus on vascular and neurological signs supplemented by investment and patient history. In most cases, dementia diagnosis requires a two-step process. First, it is important to distinguish dementia syndromes from other disorders that can resemble them, such as anxiety, delirium, and mild cognitive impairment, as is generally found, so these diseases need to be first differentiated. Second, once dementia syndrome is recognized, it is important to diagnose a subtype because it can determine the type of treatment that can be done. In general practice, the clock test is popular for cognitive screening due to its non-confrontational nature and because a clock's normal drawing excludes the presence of significant cognitive impairment more or less. The rules for scoring the tests, however, can be quite complex and using a solitary cognitive test to screen for a dementia syndrome does not do justice to the wide range of symptoms and indications that make up the clinical dementia syndrome. Daily living behaviors are measured alongside intelligence, but the measurement methods used are less reliable.[10]

DETECTION METHODS

Neuroimaging is a promising and widespread area of Alzheimer's disease detection research. Multiple brain imaging techniques can be used to classify brain abnormalities, including PET, MRI, and CT scans, which are considered preliminary disease detection tests.

Each scan involves a unique technique and detects specific structures and abnormalities in the brain and associated parts. Brain imaging is not currently a standard part of Alzheimer’s disease testing, however current clinical studies have shown promising results that may change the procedure used by physicians to diagnose the disease.

There is currently no effective treatment for Alzheimer's disease, which is the most common form of dementia, despite many years of intensive and effective research. It has become increasingly clear that if the infection is to be successfully treated, it must be identified as soon as possible, perhaps even before signs are apparent. There is therefore a great need for reliable methods of diagnosis so that Treatment to delay or avoid the disease should start to treat the disease properly as soon as possible.

PET

Positron emission tomography (PET) generates a three-dimensional color image of the human body using radiation signals. The patient is injected with a radiotracer, which is a nuclear drug related to a chemical that occurs naturally occurring chemical. Glucose is commonly used and widely used for the treatment of Alzheimer's disease drug. The radiotracer travels to the organs that use the particular energy molecule. Positrons are emitted as the compound is metabolized. The PET scan detects the energy from these positrons, converting the input to an image on the output screen. This image shows the function of the patient's body by showing how effective it is to break down the radio tracer. The amount of positron energy emitted, which reflects the extent of brain activity, creates a variety of colors and intensities. A PET scan is capable of detecting changes in the processes of metabolism, blood flow and cellular communication in the brain and other activities.[11]

CT

The computed tomography (CT) scan takes a series of cross-sectional images of the body. The individual scans are integrated into one detailed image with the help of a

computer. The CT scan provides information about tissue density in the body and in different parts of the brain to the doctor. A contrast color may be injected to provide a distinction for improved clarity A contrast coloring may be injected to distinguish similar artifacts.[12]

MRI

Techniques for magnetic resonance imaging (MRI), first used in 1977, create two or three-dimensional body images that can be used to diagnose injury and disease. The MRI system's essential component is the superconductive magnet that produces a large and stable magnetic field.[13]

CAUSES

At first, the only apparent signs of Alzheimer's disease may be increased forgetfulness or slight confusion. But over time, more of your memory is stolen by the disease, especially recent memories. The rate of worsening of symptoms varies from person to person depending on the person's age. If you have Alzheimer's, you may be the first to note that you are struggling to remember details and organize your thoughts. Or you may not recognize that anything is wrong, even if changes are noticeable to members of your family, close friends or colleagues. Three theories may describe the causes of Alzheimer's disease.

Cholinergic hypothesis

The cholinergic theory of Alzheimer's disease emerged from the combination of choline acetyltransferase and acetylcholine (ACh) deficiency findings and the fact that ACh is essential in memory and learning. Reduction in cholinergic neurons as well as cholinergic neurotransmission was thought to result in a decline in cognitive and non-cognitive functions. Loss of cholinergic function correlated with cognitive decline, but there was no causal relationship. In addition, the use of cholinesterase inhibitors (CIs) has no significant effect on more than half of patients receiving treatment with Alzheimer's disease, indicating the presence of other important processes in disease progression.[14]

Amyloid hypothesis

Amyloidosis is an abnormal tissue deposition of amyloid proteins, with altered amyloid proteins forming an insoluble ß-pleated plate. In deposits of amyloid protein, reduced tissue and cell clearance is observed. The amyloid-ß membrane protein precursor protein (APP) is proteolyzed to form Aß, and it is the amyloid form of A that makes up the amyloid plaques (neuritic plaques) present in Aß. The basis of Alzheimer's disease, according to the amyloid hypothesis, is the presence of Aß production in the brain. Evidence for the amyloid hypothesis was convincing, as amyloid-ß precursor protein (APP) encoding gene mutations were found to cause Alzheimer's family disease with significant mutation sites found in secretase and APP.[15]

Tau hypothesis

The Tau theory revolves around the existence in Alzheimer's disease of neurofibrillary tangles (NFTs). As a result of increased Tau phosphorylation (originally connected to microtubules), free tau increases with loss of functional microtubules. Phosphorylated Tau are subunits of helical paired filaments (PHFs) that form NFTs. The microtubules that are impaired affect axona Protein transport and inevitably neuronal death.[16]

TREATMENTS

Drug Therapy

Two types of drugs are used to treat Alzheimer's disease: inhibitors of acetylcholinesterase and antagonists of N-methyl D-aspartate. The two types function in various ways.

Cholinesterase Inhibitors

A person with Alzheimer's disease has lower levels of a chemical called acetylcholine in the brain. The function of acetylcholine is to send messages between nerve cells. For treat memory disorders, cholinesterase inhibitors (CI) aim to increase the supply of acetylcholine in synaptic neurotransmission. Three CIs are commonly used as the first line treatment for mild to moderate Alzheimer's disease: donepezil, rivastigmine and galantamine while donepezil and rivastigmine are both selective inhibitors; galantamine inhibits both ACh and butyrylcholinesterase. A meta-analysis collaborating randomized, double blind trials that were designed to evaluate the effectiveness and safety There was no improvement in ADL and behavior in C of CIs.

Nevertheless, the effect of donepezil and rivastigmine on cognitive functions, ADLs and behavior showed no significant difference. Similar benefits in all three medications are observed overall.[17]

NMDA Receptor Antagonists:

Memantine is a non-competitive antagonist of the NMDA receptor that is effective in treating Alzheimer's disease of moderate to severe. NMDA receptor regulation results in decreased excitotoxicity caused by glutamate. Its benefits were demonstrated in a 28-week, double-blind, parallel-group study that showed that treatment reduced patient deterioration significantly. Most adverse drug reactions were not severe and were regarded as drug-free. The positive effect on cognitive function translates into behavioral improvements: patients were less depressed and needed fewer caregivers to help improve the behavioral and emotional symptoms associated with dementia (BPSD) highlighted through a meta-analysis of 6 studies.[18]

Disease modifying treatments

While symptomatic treatments have proved helpful, it is most vital to find a cure. Since the amyloid hypothesis shows that Aß generation and deposition from

overexpressed APP cleavage constitute the fundamental basis of Alzheimer's disease, the focus of interest is on anti-amyloid therapy. Such therapies lead to lower development of Aß, higher clearance of Aß and prevention Aggregation of Aß into plaques of amyloid.[19]

Immunotherapy was also an area of interest as it aims at removing Aß peptides, which can affect cognitive decline whether directly or indirectly. Several methods can be used to achieve this by focusing on decreasing Aß generation, mainly by targeting amyloidogenic and nonamyloidogenic pathways. ß and secretases also compete for APP, with the production of ß and ß-secretase ultimately resulting in amyloid deposition and the development of APPSC soluble secretase. 2 By inhibiting ß- and ß-secretases while simultaneously potentiating ß-secretase action, Aß generation and overall deposition would be reduced. Scientists believe that a combination of genetics causes Alzheimer's disease for most people. Lifestyle and environmental factors affecting the brain over time, resulting in brain cell damage.[20]

CONCLUSION

Alzheimer's disease and its medical symptoms are briefly discussed in this article. For sequence, predementia, mild, moderate and extreme, there are four stages of Alzheimer's disease. Pneumonia, followed by myocardial infarction and septicaemia, is the most common cause of death in Alzheimer's disease. Alzheimer's disease is correlated with multiple risk factors such as age, ethnicity, employment, etc. In addition, environmental factors, vascular factors and psychosocial factors also contribute to Alzheimer disease. The techniques available for detecting Alzheimer's disease in patients include positron emission toronography, computed toronography, and magnetic resonance imaging. On the amyloid hypothesis and the cholinergic hypothesis, the cause of Alzheimer's disease can be explained.

The class of compounds used to treat Alzheimer's disease are cholinesterase inhibitors and N-methyl D-Aspartate antagonists. Future potential mechanism for treating Alzheimer's disease is the delay in neurodegeneration by targeting neuritic plaques (NPs and Neurofibrillary (NFTs).

Cholinesterase inhibitors and N-methyl D-Aspartate antagonists are the class of compounds used for treatment of Alzheimer disease. The delay in neurodegeneration by targeting neuritic plaques (NPs and Neurofibrillary (NFTs) is future potential mechanism for treatment of Alzheimer disease.

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